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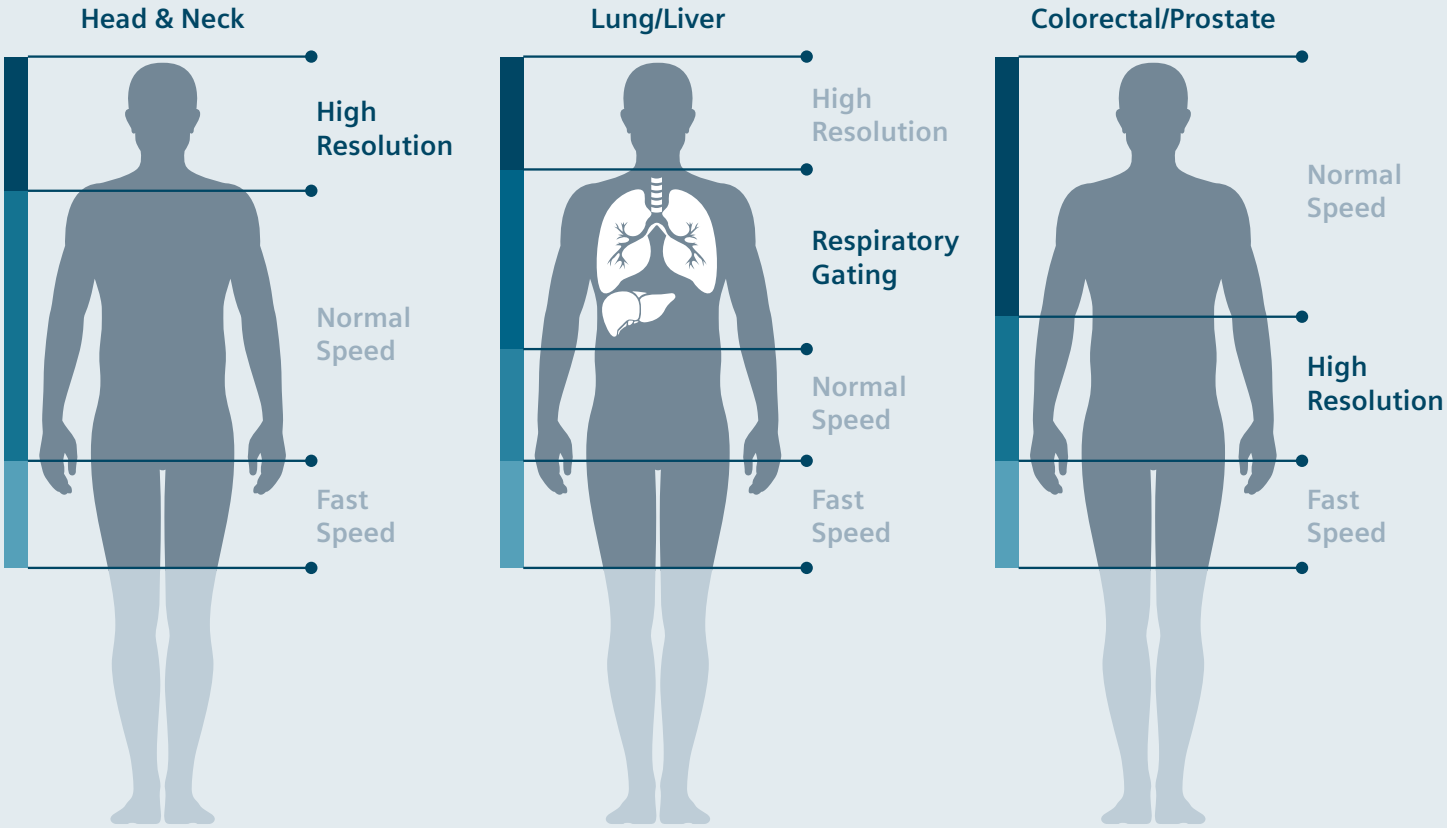

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“The system allows us to customize the scan to the individual patient by setting the speed of the table according to their clinical indications and body type.”

Dimitris Kalkanis, MD, Nuclear Medicine Specialist
Iatropolis Clinic, Athens, Greece

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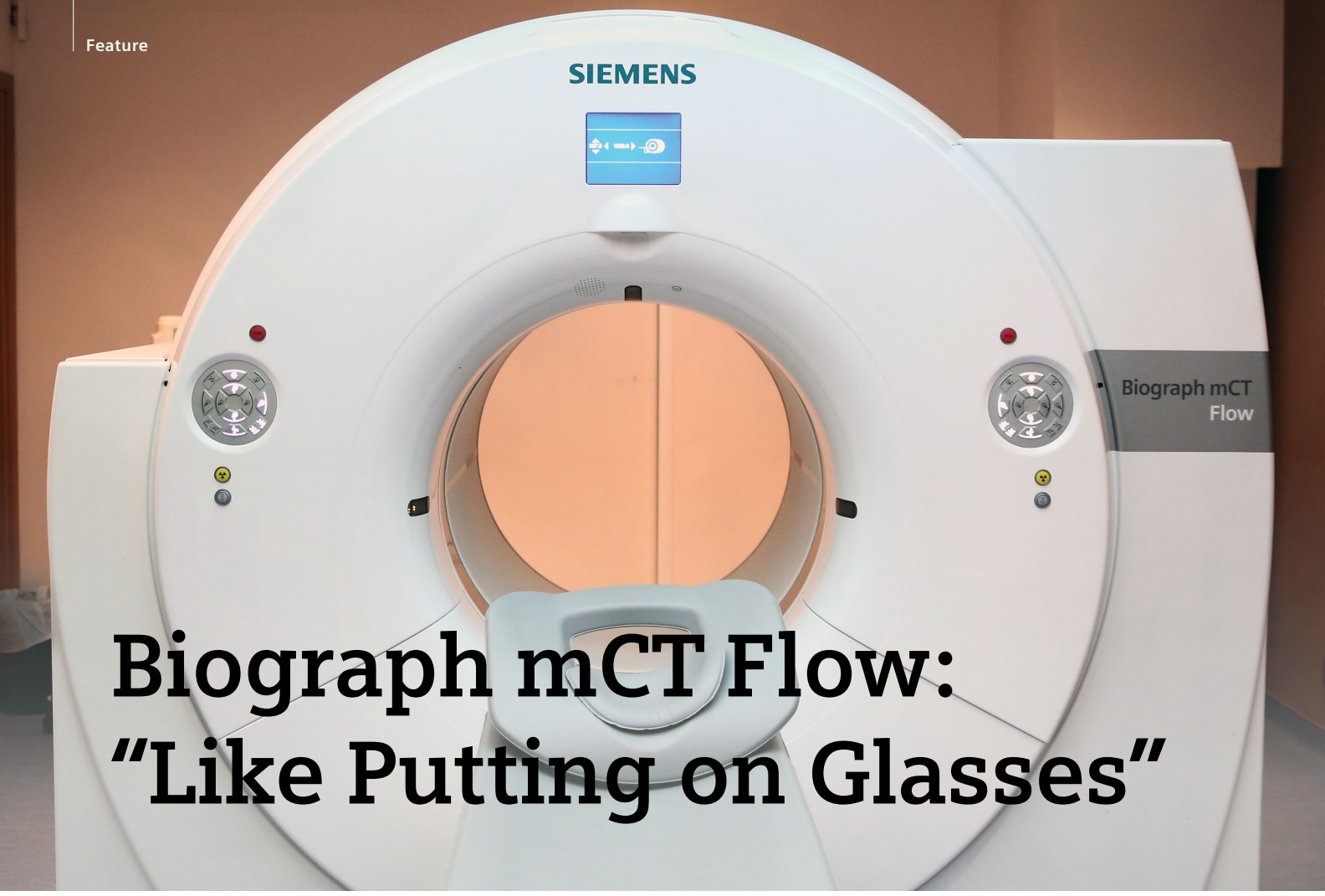

Biograph mCT Flow: "Like Putting on Glasses"

In 2014 Greece's leading diagnostic imaging group, Iatropolis Clinic, installed a Biograph mCT Flow™* PET/CT scanner, and hired two nuclear medicine specialists, Drs. Dimitrios Karantanis and Dimitrios Kalkanis, to run it. Two years later they are enthusiastic about the system—and about FlowMotion™ technology, which helps them personalize patient exams.

By Panagis Galiatsatos

Back in 1986 Chalandri was a typical northern Athens suburb, with small houses surrounded by pine trees on regular lots. The main street was home to not just one, but three, German-speaking diplomatic missions: the Swiss and GDR embassies, and the German ambassador's residence. To the north of the residence stood a multi-story building, one of the first in the area, fronted by a sign with large letters reading "Magnitiki Tomographia," the Greek term for magnetic resonance tomography. The private diagnostics imaging center operating under this name was the first in Greece to use a magnetic resonance imaging (MRI) system.

** Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 9. The full prescribing information can be found on pages 54-56.

Outside view of Iatropolis Clinic in Athens, Greece.

In the meantime, Chalandri has been swallowed up by Athens. Most of the villas along the main street have been demolished to give way to high-rises and office buildings. But the Swiss and Germans have remained. So has Iatropolis Clinic, the former Magnitiki Tomographia S.A. However, the single building has been expanded into a complex.

Even back then the name Magnitiki Tomographia was synonymous with innovation and cutting-edge medical diagnostic technology. While the Iatropolis Group has grown, it has remained true to its mission. It now runs four diagnostic imaging centers, boasting 12 MRI systems and five CT scanners, in the greater Athens area. There are another 18 departments equipped with a variety of diagnostic imaging equipment. Since 2001 the group has also set up a clinic that now offers state-of-the-art tomography and stereotactic radiation therapy for a broad spectrum of patients, as Iatropolis also works with the public health service. The 2,000 patients who come to Iatropolis every day include many people from abroad, particularly Europe and the Middle East.

FlowMotion Technology

The Iatropolis complex in Chalandri houses the Biograph mCT Flow PET/CT scanner. In 2013 Siemens introduced its innovative FlowMotion technology, which moves the patient through the system and records a continuous flow of data. Up to that point the standard practice was to do PET/CT scans in consecutive steps, the so-called step-and-shoot procedure.

In August 2014 Biograph mCT Flow went into service at Iatropolis Clinic. For Dr. Karantanis, who heads the PET/CT unit, this comes as no surprise: "Part of the group's philosophy is to be at the cutting edge of medical technology, to be as innovative as possible."

Dr. Karantanis is an expert in nuclear medicine who, like his colleague Dr. Kalkanis, specializes in PET/CT. The two work closely with radiologist Dr. Nikos Polidoropoulos on Biograph mCT Flow. In the three small rooms along the corridor leading to the PET/CT unit were patients resting before their exams. Dr. Karantanis explains that "this is a pretty busy unit, with the largest number of patients in the whole country." The clinic performs between 15 and 30 scans a day, which is a lot for a single PET/CT scanner. Currently Biograph mCT Flow conducts well over 4,000 examinations a year.

Mainly Oncological Examinations

Nearly 95 percent of exams performed at the clinic are for oncological indications. "We don't do many neurological scans, and we don't do any cardiological exams. In Greece cardiological and neurological PET/CT scans generally aren't approved by

> “The system allows us to customize the scan to the individual patient by setting the speed of the table according to their clinical indications and body type.”

Dimitrios Kalkanis, MD, Nuclear Medicine Specialist
Iatropolis Clinic, Athens, Greece

the national health service, but this is standard practice all over the world,” says Dr. Karantanis about the Greek healthcare system. “In comparison with the U.S., for example, a whole range of oncological indications don’t get approval in Greece. Our hope is that this could change in the future.”

It doesn’t take long to realize that both physicians are very glad to be able to work in this clinic with this particular system. “It’s the most modern PET technology. Our system is equipped with Time-of-Flight which gives us the greatest possible image detail,” says Dr. Karantanis. “Using this technology you can use a lower injected dose and get an image of the same or even better quality than with conventional PET/CT equipment and a higher dose. This is in everyone’s interest: we want to minimize dose for our patients, it facilitates our workflow, and enables us to use the tracer more efficiently,” enthuses Dr. Karantanis.

A “Pioneering” Technology

Both specialists praise the capabilities of FlowMotion technology. “This is a pioneering technology and it’s not available from any other company. It enables the patient table to be kept in continuous motion. Other PET/CT scanners don’t have this, but rely on bed-based imaging where the table remains still under the camera for a certain time before moving on and then stopping again, and so on. This produces a cogwheel-like movement that can lead to small artifacts in the image, which we can eliminate with FlowMotion technology,” says Dr. Kalkanis. “We’re talking about minor artifacts. But in certain table positions it can affect the sensitivity of the scan.”

Customized Examinations

Dr. Kalkanis also mentions another benefit of Biograph mCT Flow compared with conventional PET/CT scanners: “The system allows us to customize the scan to the individual patient by setting the speed of the table according to their clinical indication and body type.” This, he says, can reduce the time needed for a scan. Scans with Biograph mCT Flow are short, generally between 5 and 15 minutes. According to Dr. Karantanis, however, the ability to customize the scan has an even more important benefit: “For example if we’re looking for something specific in the chest, neck or upper abdominal area we can regulate the speed of the table so that it’s moving more slowly when these parts of the body are being scanned. That way we get as much information as possible. Basically we’re able to individualize the scan protocol for each patient. We see this as one of the great advantages of FlowMotion technology,” he explains.

The two nuclear medicine specialists believe that the reduction in scan time with Time-of-Flight and FlowMotion technologies benefits the

patient: "Patients feel better. That can potentially also mean the scan yields a better image," says Dr. Karantanis. "It's important to remember that these are generally elderly people whose health isn't so good, and who find it practically impossible to remain immobile for a prolonged period of time."

Reduction in Scan Time

Time is an important factor in a PET/CT scan. It involves injecting the patient with a radiotracer (most commonly Fludeoxyglucose F 18 or ^{18}F-FDG**). This tracer is taken up by certain tissues and emits rays that are captured by the PET detectors. However, once the tracer has been injected it takes around an hour until it has moved around the body to all the places that have to be scanned.

During this time the patient has to rest. But since the half-life of ^{18}F-FDG is only two hours, not so much time remains for the scan. This is where Drs. Karantanis and Kalkanis believe Biograph mCT Flow has another major advantage compared with conventional PET/CT scanners. "The reduction in scan time is very helpful.

Drs. Kalkanis (left) and Karantanis (right) review a PET/CT case acquired with FlowMotion technology.

It gives us plenty of time to spend with each patient without having to worry about the available tracer or other patients that urgently require a scan following tracer injection. We enjoy this luxury, and it's very important," they explain.

The course of a patient's therapy is often altered after a scan with Biograph mCT Flow. For Dr. Karantanis this stands to reason: "A scan like this is supposed to give answers in cases where conventional imaging has reached its limits. So it makes sense that a PET/CT scan, which represents state-of-the-art diagnostics, should change the course of therapy. This is the case for around 50 percent of our scans."

"Using the old, conventional PET/CT scanners in a demanding clinical environment is like being near-sighted. Using Biograph mCT Flow is like putting on eyeglasses to correct this. For the experienced eyes of radiologists and nuclear medicine physicians, the difference is tangible."

Dimitrios Karantanis, MD, Nuclear Medicine Specialist
Iatropoli Clinic, Athens, Greece

Athens-born **Panagis Galiatsatos** studied politics and history in Germany. He has been working as a journalist since 1996. Currently he is political editor at the weekly newspaper *Real News* and a business correspondent for *Neue Zürcher Zeitung NZZ*.

Both doctors are also very satisfied with the image quality and the processing capacity of Biograph mCT Flow. "We have the images as soon as the scan is finished, so we don't lose any time," they say. Referring physicians are also excited about the quality of the studies. But even more important for Dr. Karantanis is the opinion of his team, which has all the relevant information at its disposal. He sums this up with an analogy: "Using the old, conventional PET/CT scanners in a demanding clinical environment is like being near-sighted. Using Biograph mCT Flow is like putting on eyeglasses to correct this. For the experienced eyes of radiologists and nuclear medicine physicians, the difference is tangible." ■

* Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons, its future availability cannot be guaranteed. Please contact your local Siemens organization further details.

** Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 9. The full prescribing information can be found on pages 54-56.

The statements by Siemens customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption), there can be no guarantee that other customers will achieve the same results.

Fludeoxyglucose F 18 5-10mCi as an IV injection Indications and Usage

Fludeoxyglucose F 18 Injection is indicated for positron emission tomography (PET) imaging in the following settings:

- **Oncology:** For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.
- **Cardiology:** For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.
- **Neurology:** For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

Important Safety Information

- **Radiation Risks:** Radiation-emitting products, including Fludeoxyglucose F 18 Injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker.
- **Blood Glucose Abnormalities:** In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to Fludeoxyglucose F 18 Injection administration.
- **Adverse Reactions:** Hypersensitivity reactions with pruritus, edema and rash have been reported; have emergency resuscitation equipment and personnel immediately available.

Full prescribing information for Fludeoxyglucose F 18 Injection can be found on pages 54-56.

Dosage Forms and Strengths

Multiple-dose 30 mL and 50 mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) of Fludeoxyglucose F 18 injection and 4.5 mg of sodium chloride with 0.1 to 0.5% w/w ethanolas a stabilizer (approximately 15 to 50 mL volume) for intravenous administration.

Fludeoxyglucose F 18 injection is manufactured by Siemens' PETNET Solutions, 810 Innovation Drive, Knoxville, TN 39732

Image Quality Supports Higher Standards of Care for All Patients: FlowMotion

Continuous-bed-motion (CBM) scanning with Biograph mCT Flow™* translates into image quality and efficiency, shared two users, one in Lomme, France, the other in Chattanooga, Tennessee, USA. But there's a lot more to this PET/CT scanner. And it relates to the bigger picture of quality of care.

By Greg Freiherr

Alban Bailliez, MD, and colleagues in the Nuclear Medicine Department of Saint Philibert Hospital, Lomme, France, are scanning patients faster and generating images with higher resolution than was possible before they began operating Biograph mCT Flow. "We do the exams in less time and at higher quality," Bailliez said.

At a multi-hospital system with five campuses in Chattanooga, Tennessee, USA, Saima Muzahir, MD, leverages Biograph mCT Flow to provide patient-centric care by delivering exceptional data quality. "With respiratory gating, we don't have motion artifacts, which means excellent imaging and quantitation makes a difference," Muzahir said. "With the help of respiratory gating, I have improved my sensitivity and specificity in very small nodules."

The improved quality of care that results is rooted in the ability of Biograph mCT Flow to perform a deceptively simple, yet critical task—to move the patient continuously through its gantry at programmable and variable speeds.

"With respiratory gating, we don't have motion artifacts, which means excellent imaging and quantitation makes a difference."

Saima Muzahir, MD
Nuclear Medicine Physician
Chattanooga, Tenn., USA

Standardized Protocols: The Game Changer in Patient Care

Working with medical staff in Lomme, France, and Chattanooga, Tennessee, Siemens clinical specialists helped to initially set up protocols with table speeds relevant to the pathologies these sites routinely encounter. In each protocol, the table slows to allow more counts from body areas of greater interest and speeds up when covering those of lesser interest.

Both sites routinely leverage CBM, made possible through Siemens' FlowMotion™ technology, to assess patients with head and neck cancers. In these, the head and neck are scanned slowly to maximize the number of counts. Data are reconstructed into a high-resolution, 400x400 pixel matrix. Similarly scanned and reconstructed is the liver, where metastases often hide. Other body areas are scanned faster and reconstructed at lower resolution.

This approach delivers high-resolution images of the areas of greatest clinical interest, yet imposes no time penalty. The Biograph mCT Flow at Saint Philibert Hospital nets a savings of about five minutes per exam, compared to their previous PET/CT scanner.

"We now average between 15 and 20 minutes per patient," Bailliez said, "compared to between 20 and 25 minutes (with conventional PET/CT)."

Reduced complexity and greater efficiency has added capacity that can be used to serve a growing patient population. "We could explore doing up to 30 patients per day without problem," he said, noting that the current daily average is about 20.

At the Chattanooga, TN, facility, Muzahir is enthused about the respiratory gating that FlowMotion makes routinely possible for her lung cancer patients. Gating is now integrated into the base protocol, which is positively impacting the standard of care for every patient.

Its effect on standard uptake value (SUV) quantitation, Muzahir said, is remarkable. Muzahir and her colleagues recorded and then compared SUV_{max} in several patients with and without respiratory gating. "We found

a more than 50 percent difference in the values," Muzahir said. "That is a significant difference when you are trying to call something malignant versus non-malignant."

Confidence Through Consistency

Muzahir credits the acquisition approach of Biograph mCT Flow for improving data quality when assessing lung cancer, as well as the many other types of cancers seen at the Chattanooga facility, including lymphomas, melanoma and cancers of the prostate and breast. Continuous bed motion diminishes the chance of artifacts that can occur during stop-and-go scans due to overlaps between bed positions.

"Eliminating the overlapping bed acquisitions and maintaining the uniform axial noise sensitivity across the entire scan decreases the actual noise variance," she said. "This helps you better quantify the lesions based on SUV_{max}. And the reproducibility is maintained because of that."

Bailliez noted the importance of reproducibility when using Biograph mCT Flow at Saint Philibert Hospital. In conventional stop-and go scanning, he noted, data may be sampled anywhere in the field of view (FoV). If the sampling points are not the same before therapy as during or after, values may sometimes vary. Because FlowMotion protocols are built around organs rather than bed positions, the values are consistently acquired from the same locations regardless of when the exams are performed. This results in highly reproducible images and SUVs.

"We observe in our patients the same quality on the exams at different times," Bailliez said. "Because we see the same quantification values in the normal organs at those times, we are very confident that we can compare the two exams—and that we can depend on the differences we see in the SUVs."

Excellent Image Quality Without Compromise

Simplicity and dependability are key to the success of FlowMotion. Each protocol used by the French and American staff is triggered with a single click. So evident in the operation of Biograph mCT Flow, this simplicity is reflected also in the speed and ease with which staff are trained.

Other advantages accruing from FlowMotion address patient comfort and safety. One relates to what patients feel as they move through the PET/CT gantry.

"The scans are so comfortable that some patients fall asleep during acquisitions. Those who do, tend to sleep

"The scans are so comfortable that some patients fall asleep during acquisitions. Those who do, tend to sleep through the exam."

Alban Bailliez, MD
Nuclear Medicine Physician
Department of Nuclear Medicine
Saint Philibert Hospital
Lomme, France

through the exam, " Bailliez said. "They do not wake up, because the bed doesn't stop and start from one bed position to the next, as happens in conventional scanning." The sudden movements from the previous PET/CT scanner not only kept patients awake, they sometimes startled them, he mentioned, causing motion artifacts.

Muzahir notes that the fast scans possible using Biograph mCT Flow further reduces the chance of patient motion. This improves image quality, she said, and contributes to a positive patient experience.

Another advantage obtained through FlowMotion is the reduction in CT radiation dose. Because FlowMotion protocols focus on specific organs and body areas, radiation exposure is restricted to just the parts of the body being examined. In conventional scans, the CT covers the entire bed position, regardless of whether data on the whole bed is needed. The clinic staff also routinely use Siemens CARE Dose4D™, which further minimizes CT exposure.

"We systematically apply the lowest CT dose possible," Bailliez said. "We think that FlowMotion leads to optimal radiation exposure for the patient."

"We have been able to use about 15 percent lower dose," Muzahir said. "It is very important to minimize the radiation dose when you are imaging a ten-year-old who has another 50 or 60 years ahead."

Those kinds of concerns go to the root of imaging, Muzahir said.

"The idea is to deliver patient-centric care," Muzahir said. "That is our main focus." ■

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Biograph mCT Flow Uncovers World's Most Challenging Cancers

At Bad Berka Zentralklinic in Bad Berka, Germany, Richard P. Baum, MD, PhD, and colleagues diagnose and treat patients with a long misdiagnosed class of cancer, called neuroendocrine tumors. After acquiring Siemens' Biograph mCT Flow™*, Baum and colleagues can visualize neuroendocrine tumors smaller than they have ever been able to see before, in a shorter amount of time.

By Greg Freiherr

Lying face up, prepped to be scanned with PET/CT at the Bad Berka Zentralklinic, patients see the sky as they might if they were outside, a mural complemented by painted walls that bear a striking resemblance of the pastoral landscape that surrounds this modern hospital complex. Established over a half-century ago as a tuberculosis sanatorium, Bad Berka Zentralklinic now houses a center of excellence for some of the most diagnostically challenging cancers.

They are called neuroendocrine tumors (NETs), but they are not found only in the brain. Most inhabit the gastro-entero-pancreatic system, but they can originate anywhere in the body—small intestines, adrenals, pituitary, pancreas or lung, according to Baum, Chairman and Clinical Director of the Theranostics Center for Molecular Radiotherapy and Molecular Imaging.

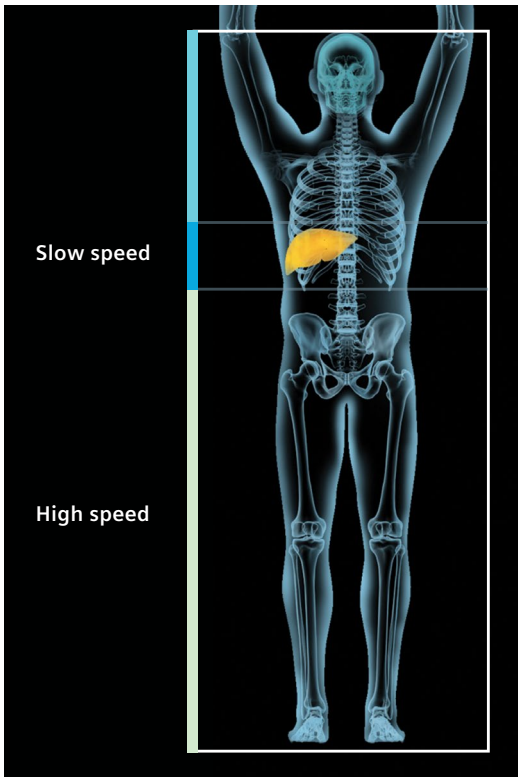
Symptoms can mimic those of other diseases. The diarrhea from NETs may often be attributed to irritable bowel syndrome; respiratory distress to bronchial asthma; facial redness from excess hormone production to alcoholism.

"It is a very heterogeneous disease, ranging from very slow growing tumors to ones that can lead to death in a few months," he said.

When it comes to NETs, Baum is one of the world's leading experts. He joined the Zentralklinic when PET was a solo modality, not a hybrid. Early on, Baum spearheaded the use of PET and SPECT, establishing in Bad Berka the practice of radiotherapy in combination with diagnostic and prognostic molecular imaging, a combination he calls theranostics. "It is an artificial word that says you can determine the best

Richard P. Baum, MD, PhD, Chairman, Theranostics Center of Molecular Radiotherapy and Molecular Imaging (PET/CT) (right); Franz C. Robiller, MD, Chief, Center of Molecular Imaging (PET/CT) (left); and Coline Lehmann, MD, senior physician (middle), in the Biograph mCT Flow scanner room in which patients see a mural of the sky painted onto the ceiling.

** ^{68}Ga biomarker referenced herein is not currently recognized by the US FDA as being safe and effective, and Siemens does not make any claims regarding its use.



FlowMotion's variable table speed allows physicians to tailor scan protocols specifically for each patient that not only minimizes the overall patient exposure to radiation, but delivers image resolution suited for specific regions.

therapy by using a diagnostic molecular imaging tool—PET/CT with biomarkers that target receptors in the neuroendocrine tumors," he said.

FlowMotion Arrives

In early 2014, the clinic acquired Siemens' advanced PET/CT scanner, Biograph mCT Flow, which replaced their Siemens Biograph™ Duo. With this new system, scans with ^{68}Ga-based biomarkers**, produced in a generator at the Bad Berka Zentralklinic, are done in minutes.

Images delivered by Biograph mCT Flow can show some of the tiniest lesions; standard uptake values (SUVs) indicate the activity of the tumor, thus allowing quantitative measures that buoy the qualitative.

Once the tumors are found, additional scans, measuring glucose metabolism, help distinguish between fast and slow growing tumors. Hypermetabolic lesions indicate fast metabolism and growth. While hypometabolic lesions indicate the tumors are growing slowly.

Using both scans helps provide physicians critical information to come up with the broad outlines of a treatment plan.

Precise localization, achieved through Biograph mCT Flow, allows planning for biopsy from which a histopathologic report is prepared. Following treatment, PET/CT tracks patient response, potentially allowing for mid-course corrections in dose or approach. Finally, on follow-up scans, the sensitivity of Biograph mCT Flow in combination with the specificity of ^{68}Ga biomarkers allows Baum and colleagues to spot early signs of recurrence.

Unlike conventional PET/CT scanners, Biograph mCT Flow, propelled by Siemens' unique FlowMotion™ technology, scans continuously from one point to another, canvassing the body in a single movement. The speed of the continuously moving table, as defined by the operator, may slow as one area passes through the detector rings, for example, the liver. This allows more counts to be gathered from an area suspected of harboring a cancer, heightening the resolution. The table might then accelerate when scanning another area of lesser concern, where lower resolution images are enough.

Protocols Enhance Visualization

^{68}Ga-based-PET imaging is specific to NETs, providing "good target-to-non-target ratios," Baum said. Special protocols are applied, however, to reduce respiratory and cardiac motion. These protocols may involve data acquisition during a single-breath-hold. Or they may acquire cardiac data selectively using diastolic and systolic triggers. This is especially important for the five to ten percent of patients with NETs who have myocardial or pericardial metastases.

One such patient had a huge myocardial metastasis in the apex of the heart, Baum recalled. The tumor was resected and PET/CT with Biograph mCT Flow was then performed on follow-up to determine whether the lesion was removed completely.

"In this case we were able to confirm that there was complete resection," Baum said. The scan unveiled, however, a small lesion in the lymph node behind the heart, as well as a metastasis in the liver. "With Biograph mCT Flow, we have very good sensitivity for detecting small lesions and also through cardiac gating, we can get better resolution for disease in and around the heart, " he said.

Attesting to the value and utility of Biograph mCT Flow, about 1,200 studies were done on Biograph mCT Flow in the first four months since it began operating in the end of February 2014—an average of almost 14 per day. Of these, about 40 percent involved NET patients. The rest were suspected or known to have other cancers, frequently of the lung but also colorectal, prostate and brain. Leveraging their

"Every patient coming to therapy has a PET/CT with our Biograph mCT Flow; it is an absolute requirement."

Richard P. Baum, MD, PhD, Chairman & Clinical Director
Theranostics Center for Molecular Radiotherapy & Molecular Imaging
Bad Berka Zentralklinic, Bad Berka, Germany

facilities capabilities, Baum's team produces a dozen different PET radionuclides for brain tumors and, of course, ^{68}Ga for NETs. And these are only the ones used in diagnosis.

On the front lines of the battle with neuroendocrine cancers are therapeutic compounds that are radiolabeled somatostain analogs, part of peptide receptor radionuclide therapy (PRRT).

Accurate Routine Use

"Every patient coming to therapy has a PET/CT with our Biograph mCT Flow; it is an absolute requirement," he said. "With PET/CT we can most accurately determine the spread of the disease."

Although inherently advantageous, the increased sensitivity of Biograph mCT Flow can complicate the interpretation of qualitative images and quantitative measures acquired on a patient over time. The most recent SUVs may be higher and images brighter than those acquired on preceding scanners, not because the tumor is absorbing more radionuclide but because Biograph mCT Flow is recording more counts.

Baum and his colleagues have been making adjustments by calculating tumor counts in relation to ones in the spleen, which also contains cells with a lot of somatostatin receptors. Calculations provide a ratio indicating the greater sensitivity of the PET/CT scanner for the individual patient.

Baum also suggests a means to cross calibrate scanners using phantoms, a technique used in Siemens' *syngo*®.via for Molecular Imaging EQ•PET algorithm, which allows physicians to calibrate studies performed on PET/CT scanners made by different vendors.

"I think this is very important because patients will undergo imaging at different institutions with different scanners and if you use the concept of molecular response based on tumor uptake of the radionuclide to adjust therapy, you need this cross calibration of scanners," he said.

With Biograph mCT Flow, patients can be scanned in 10 to 15 minutes including respiratory gating, according to Baum. "I am a real fan of this high-resolution Biograph mCT Flow because it is fast; it is very convenient for the patient; and it has a wide gantry," Baum said.

Siemens' latest PET/CT scanner shows much smaller lesions compared to the clinic's previous system, according to Baum. "It has a better reconstruction algorithm so we have sharper images," he said. "We can be more confident."

Improved image quality is especially helpful to physicians new to the diagnosis of neuroendocrine tumors. "If you have very small lesions and not so much uptake (by the tumors), you have different opinions," he said. "That is where Biograph mCT Flow has made the most dramatic improvement. Doctors having these sharper images and better contrast can more often make the correct diagnosis."

The sensitivity and resolution of Biograph mCT Flow is proving important in the assessment of other oncology patients, particularly those with prostate cancer. "You can detect very small tumor lesions, very small lymph node metastases in patients for re-staging after primary tumor resection with rising PSA," he said.

A Storied History Unfolds

The Zentralklinic has 669 beds. It was built in 1952 as a treatment center for tuberculosis. Staffed by 1,600 employees, it is the largest employer in the region around Bad Berka, a spa town of some 8,000 located on the Ilm River. Included are 22 beds in the nuclear medicine department dedicated to patients undergoing radiotherapy. German law mandates 48-hour stays for anyone undergoing radiotherapy. For this reason, the Theranostics center reports 90 percent occupancy, a rate that Baum said is misleadingly low. Many patients, if possible, time their stay so they can go home before the weekend.

The Theranostics Center for Molecular Radiotherapy and Molecular Imaging, which Baum heads, is a European Neuroendocrine Tumor Society Center of Excellence known worldwide for its ability to discern the otherwise indiscernible. The incidence of NETs has been underestimated, according to Baum, because of the diagnostic quandary they impose.

"They are the second most common gastrointestinal cancer, surpassed only by colorectal cancer, and more frequent than pancreatic adenocarcinomas or gastric cancer or hepatobiliary cancers," Baum said.

NETs could occur annually in as many as five per 100,000 people. Prevalence may be greater still, possibly eight times greater, he said. This is so because many NETS are slow growing. Patients can live 20 years before symptoms appear and even then interpreting clinical signs typically is not easy, a reality that further confounds their diagnosis, as physicians apply the tenet of thinking horses not zebras at the sound of hooves.

"About 50 percent of patients with small intestinal neuroendocrine tumors are misdiagnosed as having irritable bowel syndrome, because they have diarrhea," he said. "They are misdiagnosed as having allergies, for example to gluten. Tumors that produce serotonin cause the red face associated with alcoholism. Or increase blood pressure, which then doctors believe is the cause of their other symptoms."

Their tumors may also produce excess insulin, causing hypoglycemia. "These patients can end up in the psychiatric unit because hypoglycemia causes 'crazy' symptoms; others cause ulcers of the stomach," he said.

The value of PET/CT in the discovery of NETs is indisputable. When the etiology of a neuroendocrine cancer cannot be otherwise determined, PET/CT can help physicians find the primary tumor in 59 percent of NETs, according to Baum, a percentage calculated on the basis of collaborative research performed by his and another team in Italy.

"So in nearly two thirds of the patients, we are able to detect the primary tumor and this is very important because resection of the primary tumor at least in the small bowel improves survival," Baum said.

PET/CT Stimulates Thought

Specialists at the Zentralklinic work with Baum and his radiological colleagues to craft patient-specific therapies. This multi-disciplinary tumor board (MDB) is comprised of more than a dozen specialists, representing gastroenterology, endocrinology, internal medicine, interventional radiology and surgery. The board discusses each case to determine the best therapy for the individual, Baum said. And while there may be many considerations, all discussions begin the same. "We would never start any patient discussion in the MDB without results from a PET/CT scan," Baum said.

Sometimes the calculus is simple. "If you see one lesion, the case goes to the surgeon," he said. "If you see two or three in the liver, it probably goes to the interventional radiologist. If you have lesions all over—in the bone, in the lymph nodes—the patient goes to the nuclear medicine ward for PRRT."

One such case was a 32-year-old woman with pancreatic neuroendocrine tumors. PET/CT showed a large mass in the pancreas and bulky lymph node metastases compressing the aorta and mesenteric artery. The MDB judged the case inoperable and the patient was sent for PRRT. Ultimately, this therapy reduced the tumor burden enough that surgery became an option. Pancreatic and lymph node tumors were then resected.

Regularly scheduled PET/CTs over the next five years showed no sign of recurrence. But then, in November last year, a follow-up PET/CT uncovered two small—less than 1.5 cm—lymph node metastases. A PRRT injection of lutetium-177 (^{177}Lu) lit up the lesions and, using a gamma probe intraoperatively, the surgeon found and resected the lesions. In early summer, the patient returned for a six-month follow-up.

"The PET/CT revealed she was again tumor free," Baum said.

This most recent scan was done on Biograph mCT Flow, enhancing Baum's confidence that the surgery was successful.

"Biograph mCT Flow delivers very high resolution and brilliant images," he said. "It detects many more small lesions." ■

* Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

** ^{68}Ga biomarker referenced herein is not currently recognized by the US FDA as being safe and effective, and Siemens does not make any claims regarding its use.

The statements by Siemens customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption), there can be no guarantee that other customers will achieve the same results.

Think Whole-body Dynamic PET Imaging is for Research Only?

Perhaps it's Time to Re-evaluate

With the introduction of continuous bed motion technology, whole-body dynamic PET imaging becomes more practical in clinical routine, and less cumbersome in research settings. Recent research undertaken by Koji Murakami, MD, PhD, demonstrates this, which raises the question: Are we at the advent of a paradigm shift?

By Carl von Gall, MD, Molecular Imaging Business Line, Siemens Healthcare

Since the beginning of positron emission tomography (PET), researchers worldwide have tried to understand the processes underlying the uptake, metabolization, trapping and binding of PET tracers. The preferred method of study has been dynamic PET acquisition (dPET), whereby tracer distribution is acquired over time, typically, from a single bed position. From that continuously acquired data, different time frames are then reconstructed.

However, results have been difficult to reproduce, due to individualized approaches to acquisition time, reconstruction methodology and analytical techniques. Thus, dPET has become a heterogeneous field, which limits its feasibility in both clinical routine use and research settings.

From the clinical routine perspective, institutions faced several obstacles, even when incorporating facilitated dynamic approaches. Take dual time-point imaging, for example: Protocol setups varied because they were developed according to the designs of the individual institutions and investigators. Subsequently, none of them fit into daily routine environments because of the high individualization and, therefore, lack of standardization. Without standardization, the complexity of patient handling and imaging made dPET impractical in routine use, especially for institutions with high patient throughput.

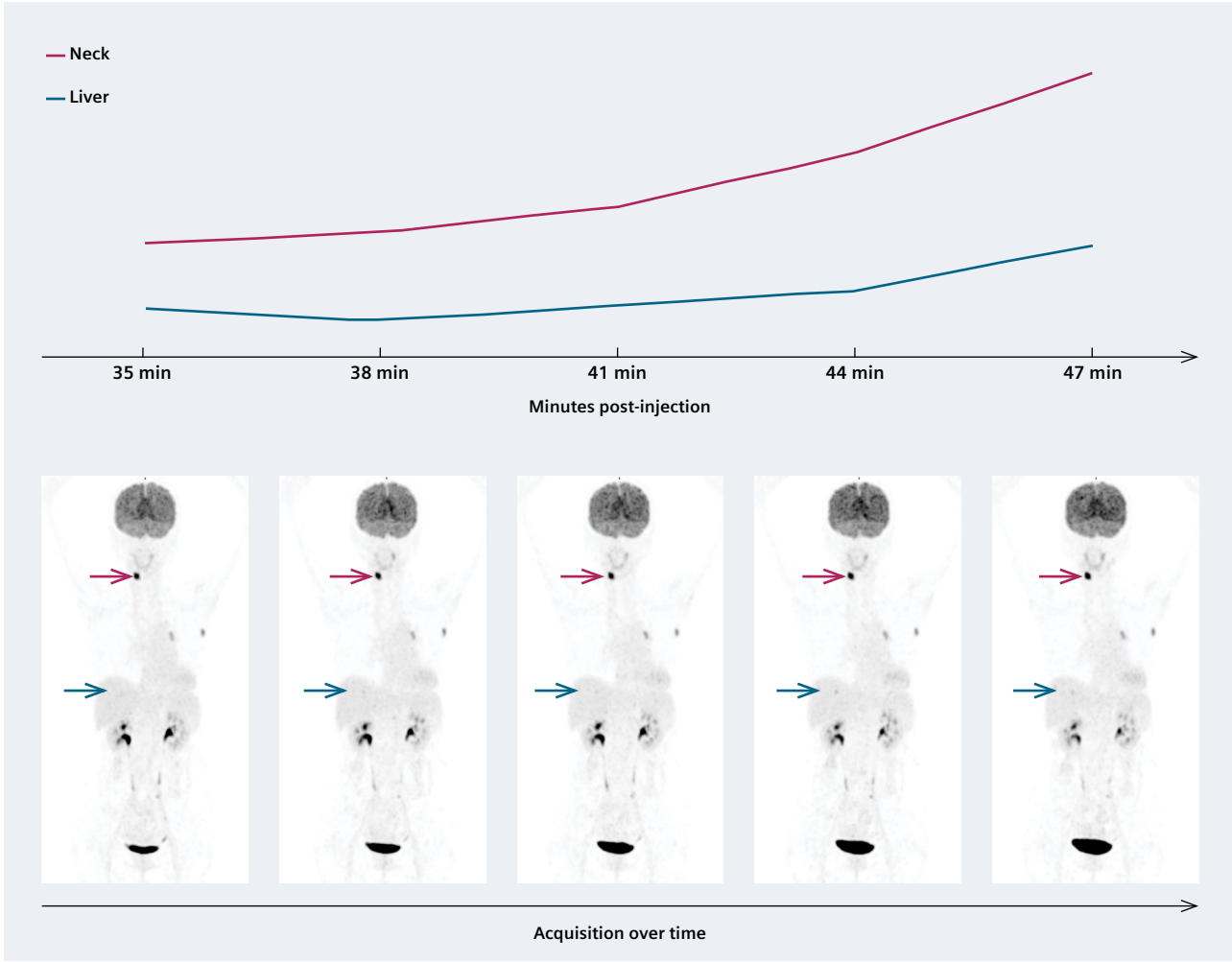
From the researcher's perspective, dynamic acquisitions of important lesions or organs were only possible if they all fit in the axial field of view (FoV). For most scanners, the FoV spanned between 15 to 21 cm. Due to this limitation, especially in distant lesions or peripheral foci, dPET acquisition is cumbersome and can sometimes be close to impossible.

This changed with the introduction of Biograph mCT Flow™* with FlowMotion™ technology. Implementing continuous bed motion as its core feature, physicians can acquire dPET in a new way: Whole-body dynamic imaging.

Whole-body dynamic imaging allows the user to overcome the limitations in conventional dPET. It enables dynamic acquisition over the entire scan range by continuously moving the patient in the axial orientation with a defined number of passes until the targeted time period is completed. With this, whole-body dynamic imaging extends the capability of dPET from the FoV to the field of interest. And as such, clinical physicians and researchers may overcome the range limitation and include regions of the body into one dynamic acquisition that used to be out of reach.

Having the capability to consider the bed movements into the acquisition and reconstruction with variable table speed provides a great variety of examination protocols. From shortened dPET protocols and quick time activity curve analysis with *syngo*®.via PET/CT Oncology Engine Pro, to third-party analysis tools. Whether it is tracer distribution in a lesion over time, gathering more inside information of a drug's pathway through the body or tracing the metabolic patterns in multiple organs at the same time over a large FoV, it all becomes easily accessible in a single protocol at the click of a button.

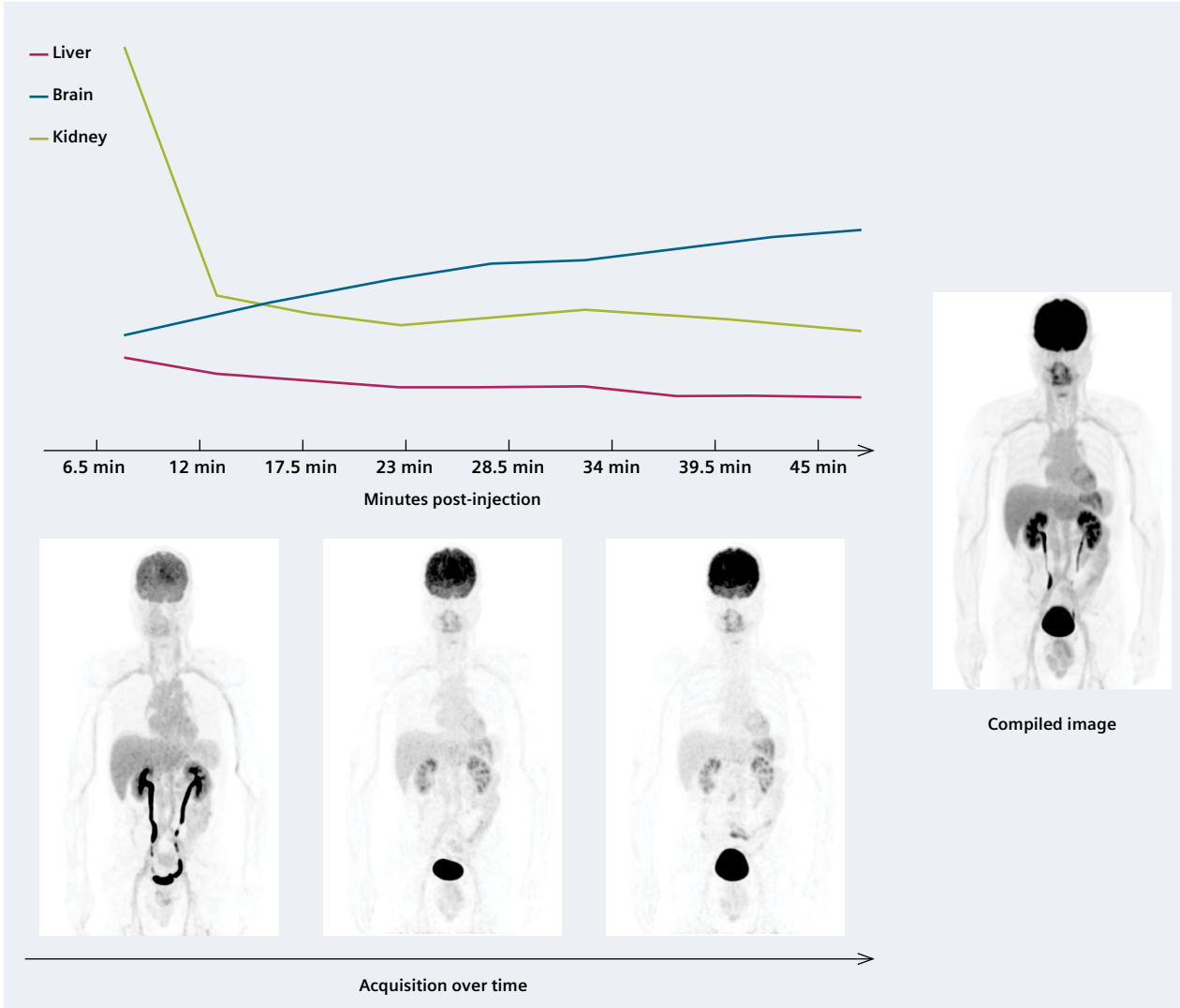
One of the early adopters of whole-body dPET imaging is Koji Murakami, MD, PhD, who is Head of the Division of Nuclear Medicine in the Department of Radiology at Keio University School of Medicine, Tokyo, Japan.



Focally altered metabolism in a patient with malignant disease dynamically acquired 47 minutes post-injection. The graph (top) displays the counts measured in a 1 cm VOI placed over a cervical lesion (*red arrow*) and demarcates liver lesions over time (*blue arrow*). The bottom shows the corresponding whole-body images. Data courtesy of the Department of Radiology, Keio University School of Medicine, Tokyo, Japan.

“With FlowMotion, we obtained a major tool to analyze dynamic studies without limitation to one bed position.”

Koji Murakami, MD, PhD, Head of Nuclear Medicine, Department of Radiology
Keio University School of Medicine, Tokyo, Japan



Physiological uptake in a healthy subject dynamically acquired over 45 minutes post-injection. The graph (top) displays the counts measured in a 1 cm VOI placed in the liver, brain and kidney parenchyma on one side. Note the differences in tracer elimination and uptake over time. The bottom shows the corresponding whole-body images with a compiled whole-body of all time frames (*right*). Data courtesy of the Department of Radiology, Keio University School of Medicine, Tokyo, Japan.

Since 2014, Murakami's department has used Biograph mCT Flow and FlowMotion for facilitated respiratory gating and standardized protocols. As a result, Murakami and colleagues have experienced increased uniformity and reduced noise, while maintaining SUV and image quality. Murakami presented the results of his team's work at the European Association of Nuclear Medicine (EANM) Congress 2015 in Hamburg, Germany.

Murakami expanded his use of FlowMotion by taking advantage of the whole-body dynamic feature in his oncological patient setting. Just by the first image series, Murakami felt excited:

"Unlike most CT or MR examinations, the time axis is very important in nuclear medicine. But particular to the field of oncology, sometimes we have to obtain a very long axial field of view to cover all lesions. With FlowMotion, we obtained a major tool to analyze dynamic studies without limitation to one bed position."

Notably his department has experimented with dPET studies of varying length. The researchers have conducted early-series studies, acquiring data soon after injection of the PET tracer, for example, from 30 to 360 seconds post-injection. They have also performed delayed dPET studies spanning 20 minutes.

Recently, the research team has been comparing conventional whole-body PET to compiled whole-body dynamic PET studies. The goal is to document and establish the value of dPET in routine use, and to potentially replace additional static acquisitions in future reporting.

"First we need to determine if we may discriminate additional uptake," Murakami said. "But the objective in the mid-term is to differentiate or improve the diagnosis by analyzing the time-activity curve of a specific disease, and even further, of each individual lesion."

To this end, Murakami has received funding to continue performing research into dynamic PET and expand on studies into compiled imaging as a means to improve routine clinical workflow and further define pathological alterations in glucose metabolism.

Considering Murakami et al.'s promising initial results and acknowledging that, before FlowMotion, whole-body dPET was impractical, there is reason to believe this approach could bring dPET into clinical routine.

Is this the advent of a paradigm shift? We believe the first steps are made. ■

* Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons, its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

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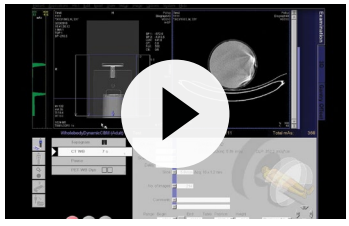
Setting up dynamic PET protocols

See how easy it is to set up a dynamic PET protocol with FlowMotion.

To watch the video, scan the QR code using the reader app on your smartphone or enter the URL into your internet browser.

siemens.com/dpet-protocol-setup



Case 1

Improved Visualization of Solitary Para-aortic Metastases in a Patient with Operated Uterine Cancer Using Hi-Rez Reconstruction and FlowMotion Acquisition

By Dustin Osborne, PhD

Data courtesy of the University of Tennessee Medical Center, Knoxville, Tenn., USA

History

A 69-year-old woman with a history of uterine carcinoma treated with hysterectomy presented with progressively increasing serum CA-125. Because tumor recurrence or metastases were possible, the patient was referred for a Fludeoxyglucose F 18 (^{18}F-FDG)* PET/CT study. The study was performed on a Biograph mCT Flow™**

1 hour following an IV injection (10 mCi) of ^{18}F-FDG. FlowMotion™ acquisition was performed using a slower table speed (0.3 mm/sec) on the middle and lower abdomen and pelvis for higher count statistics. The head, neck and thorax were acquired at a regular speed (0.7 mm/sec), while the extremities were acquired at a faster speed (1.5 mm/sec).

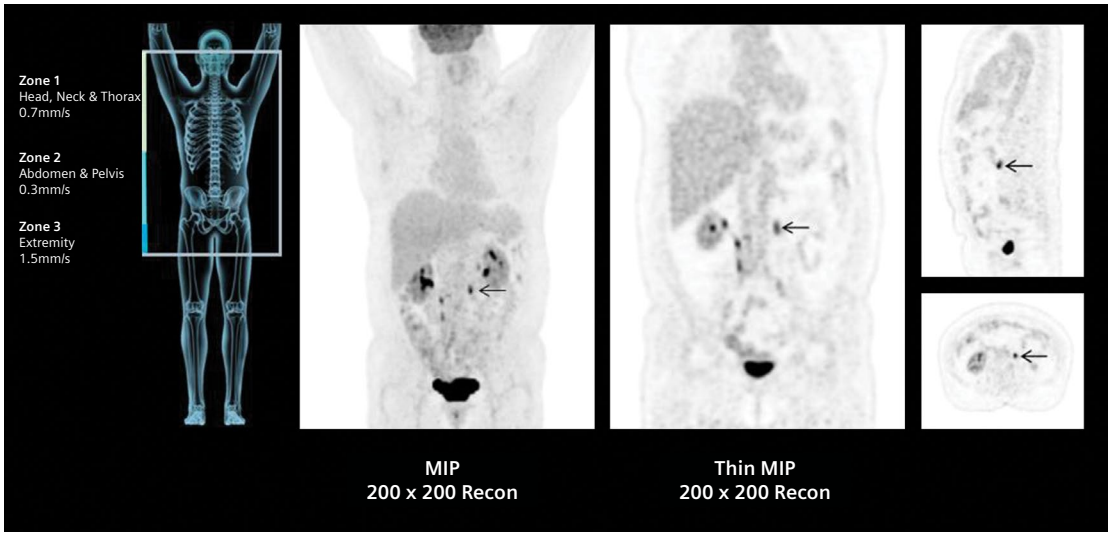


Figure 1: Whole-body 200 x 200 matrix PET reconstructions show focal hypermetabolism in the para-aortic region that is suspicious for metastases.

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

Diagnosis

Whole-body PET images (*Figure 1*) showed focal hypermetabolism in the para-aortic region, medial to the left renal hilum, which suggested left para-aortic lymph node metastases. No other well-defined, abnormal focal hypermetabolic lesion was visualized. The left ureter had some ^{18}F-FDG retention in the middle third that was visible in the PET image. The regions of the abdomen and pelvis that were acquired with slower table speeds—in order to achieve higher count statistics—were reconstructed with a higher 400 x 400 matrix. When compared to standard 200 x 200 whole-body reconstructions, Hi-Rez 400 x 400 reconstructions demonstrated sharper delineation and higher lesion contrast in the small left para-aortic lymph nodal metastases. This difference was achieved through decreased partial volume effects that were obtained with smaller voxel dimensions obtained with higher resolution reconstruction. Figure 2 and 3 demonstrated the sharp definition of the para-aortic nodal metastases (*arrows*) from the Hi-Rez reconstruction, while the same lesion appeared slightly elongated with lower lesion-to-background contrast in the standard 200 x 200 matrix reconstruction. No additional nodal metastases or tumor recurrence were visualized in either reconstruction.

Comments

In a patient with operated uterine carcinoma, suspicious of metastases due to gradual increase in serum markers, PET/CT helped delineate solitary left para-aortic nodal metastases. Although the lymph node was borderline enlarged on the CT, hypermetabolism on PET/CT was crucial for proper characterization of the lymph nodal metastases. This example demonstrated the value of ^{18}F-FDG PET/CT in the detection of small metastatic foci during post-operative follow-up for the uterine carcinoma. Because of the small size of the metastatic lesion, local radiation therapy was preferred. In some clinical trials, though, combination chemotherapy has been proven to be useful when the tumor burden is small. Thus, the detection of this para-aortic metastatic lesion by PET/CT was critical to subsequent management decisions.

High-resolution PET imaging helps detect small lesions, often with lower levels of ^{18}F-FDG uptake, by decreasing the partial volume effects through the reduction of voxel dimensions with sharper delineation of lesion margins and higher lesion contrast, as seen in this clinical example. This helps provide a higher diagnostic confidence for lesion detectability. Since early detection of small metastatic foci is critical for a successful management approach, high image quality and resolution of PET/

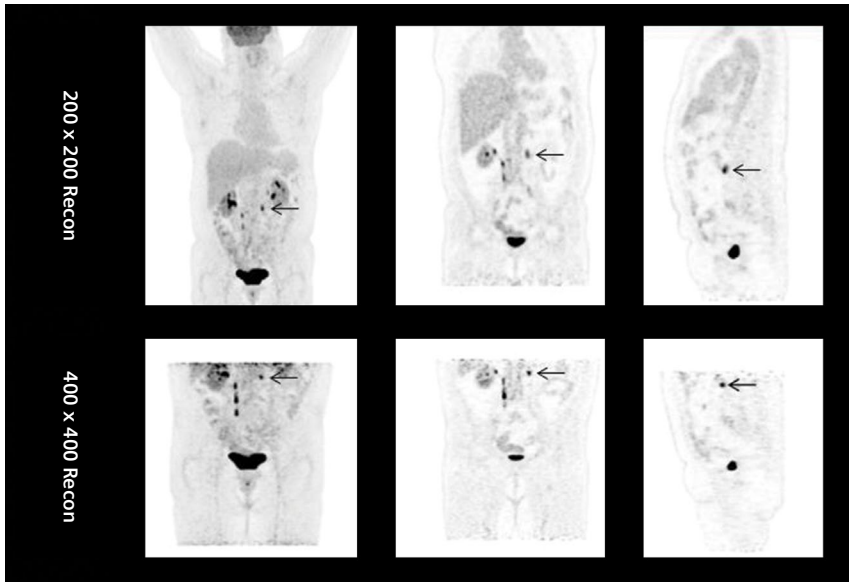


Figure 2: Comparison of 200 x 200 and 400 x 400 matrix PET reconstructions show sharper delineation and higher lesion-to-background contrast in solitary left para-aortic lymph node metastases (*arrows*).

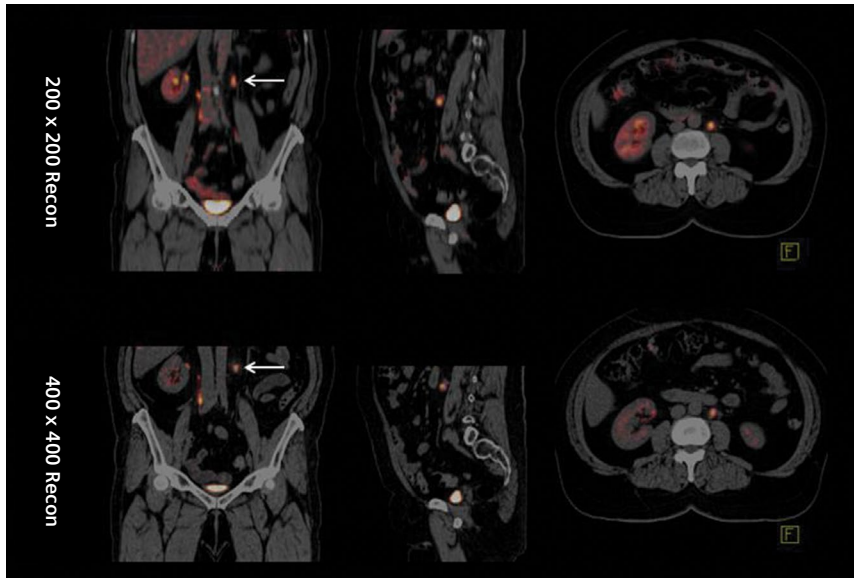


Figure 3: Fused PET/CT images show sharper delineation of left para-aortic lymph node metastases with Hi-Rez reconstruction.

CT is key for diagnostic confidence. Using ^{18}F-FDG PET/CT with integrated contrast-enhanced CT in 90 patients with treated uterine carcinoma and suspected recurrence, Kitajima et al.[1] demonstrated a lesion-based sensitivity of 90.5% and a specificity of 99.5%. The false negative lesions on PET/CT in this study were mostly pelvic and para-aortic lymph node metastases, which were less than 5 mm in size. These lesions were too small, with too low ^{18}F-FDG uptake to be detected with PET/CT. High-resolution reconstructions of PET acquisitions with high count statistics and lower partial volume effects, along with improved lesion contrast achieved with Time-of-Flight and point-spread-function (PSF) reconstruction, could potentially improve the detectability of such small lesions, and thereby improve the sensitivity of PET/CT for recurrence detection in uterine carcinoma (in the case of Kitajima et al.).

Conclusion

FlowMotion acquisition enables acquisition of flexible ranges with slower table speeds in order to achieve higher count statistics—necessary for higher matrix reconstruction. In this example, the mid- and lower abdomen and pelvis were acquired with slower table speeds, since those were the regions of interest in the patient with uterine cancer. Subsequently, those regions were reconstructed with a higher matrix. Flexibility with FlowMotion enables optimized imaging protocols, tailor-made to the patient's clinical requirements without undue time penalty. ■

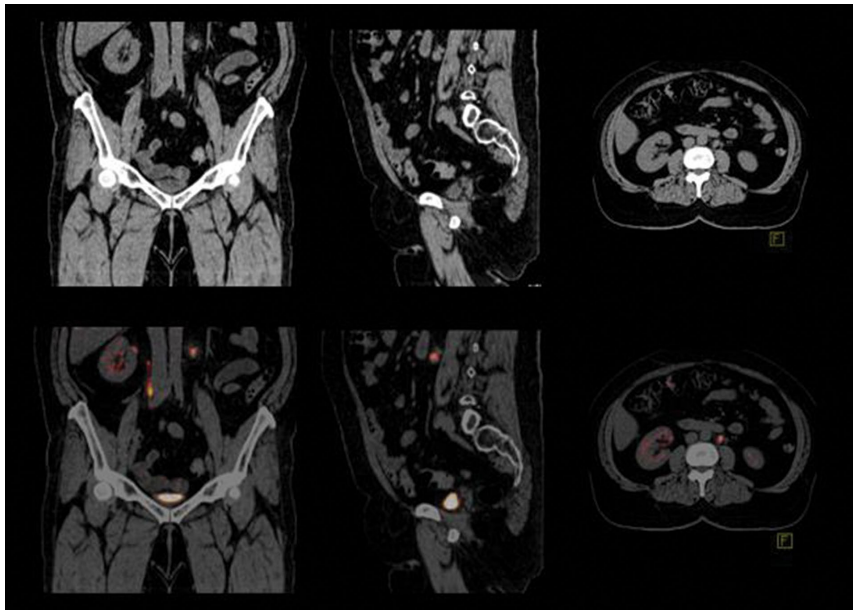


Figure 4: Thin-slice CT and fused PET/CT images help delineate small solitary hypermetabolic left para-aortic nodal metastases.

Examination Protocol

Scanner: Biograph mCT Flow

PET	
Injected dose	370 MBq (10 mCi) ^{18}F-FDG
Scan delay	60 min post injection
Scan speed	Zone 1, 0.7 mm/sec; Zone 2, 0.3 mm/sec; Zone 3, 1.5 mm/sec
Acquisition	FlowMotion, continuous bed motion with variable speeds

CT	Non-contrast
Tube voltage	120 kV
Tube current	40 eff mAs
Slice collimation	2.5 mm
Slice thickness	5 mm

References:
[1] Kitajima et al. Eur J Nucl Med Mol Imaging. 2009; 36: 362-372.

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

** Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

Fludeoxyglucose F18 5-10mCi as an IV injection
Indications and Usage

Fludeoxyglucose F 18 Injection is indicated for positron emission tomography (PET) imaging in the following settings:

- **Oncology:** For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.
- **Cardiology:** For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.
- **Neurology:** For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

Important Safety Information

- **Radiation Risks:** Radiation-emitting products, including Fludeoxyglucose F 18 Injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker.
- **Blood Glucose Abnormalities:** In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to Fludeoxyglucose F 18 Injection administration.
- **Adverse Reactions:** Hypersensitivity reactions with pruritus, edema and rash have been reported; have emergency resuscitation equipment and personnel immediately available.

Full prescribing information for Fludeoxyglucose F 18 Injection can be found on pages 54-56.

Dosage Forms and Strengths

Multiple-dose 30 mL and 50 mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) of Fludeoxyglucose F 18 injection and 4.5 mg of sodium chloride with 0.1 to 0.5% w/w ethanolas a stabilizer (approximately 15 to 50 mL volume) for intravenous administration.

Fludeoxyglucose F 18 injection is manufactured by Siemens' PETNET Solutions, 810 Innovation Drive, Knoxville, TN 39732

Case 2

Improved Characterization of Small Solitary Lung Nodule Using HD•Chest and FlowMotion in a Patient with Rectal Carcinoma

By Partha Ghosh, MD, Molecular Imaging Business Line, Siemens Healthcare

Data courtesy of Royal Brisbane Hospital, Brisbane, Australia

History
A 61-year-old male patient with a history of rectal carcinoma treated with recto-sigmoid resection and partial hepatectomy for solitary liver metastases underwent Fludeoxyglucose F 18 (^{18}F-FDG)* PET/CT for a follow-up.

The PET/CT study was performed on Biograph mCT Flow™**. Following non-contrast whole-body CT, the PET acquisition was performed with variable table speed. The liver and upper abdomen were acquired through integrated respiratory gating, with faster acquisition for the extremities in order to optimize acquisition time.

The whole-body PET study was reconstructed as a non-gated 200 x 200 matrix reconstruction. However, the gated data from the thorax and upper abdomen were reconstructed as HD•Chest with 33% duty cycle in order to obtain relatively motion-free images of the lung for improved evaluation of lung lesions.

Diagnosis
Coronal MIP and thin MIP images of the whole-body PET study showed a solitary focal hypermetabolic nodular lesion in the lung, which was suspicious for malignancy with an SUV_{max} of 2.9 in the non-gated study. The surgical resection bed in the anterior part of the left lobe of the liver showed normal tracer uptake. Both the renal pelvis and left upper ureter show tracer retention. Mild ^{18}F-FDG uptake in bilateral inguinal nodes was likely to be reactive.

The HD•Chest reconstruction of the respiratory-gated data of the lung, which is now part of the single scan protocol due to the use of FlowMotion™, demonstrated sharper delineation of the hypermetabolic lung nodule with higher lesion conspicuity and increased target-to-background as compared to the non-gated acquisition.

Quantitative comparison between non-gated reconstruction and HD•Chest showed substantially higher SUV_{max} with HD•Chest compared to that obtained from the non-gated reconstruction. SUV_{max} increased from 2.97 to 3.65 with HD•Chest, an increase of 23%. This can be attributed to the lack of peripheral blurring and smaller lesion dimension achieved with HD•Chest by eliminating the respiratory motion artifacts. The SUV_{max} level was consistent with a diagnosis of malignancy in the pulmonary nodule, possibly secondary to lung metastases from rectal carcinoma.

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

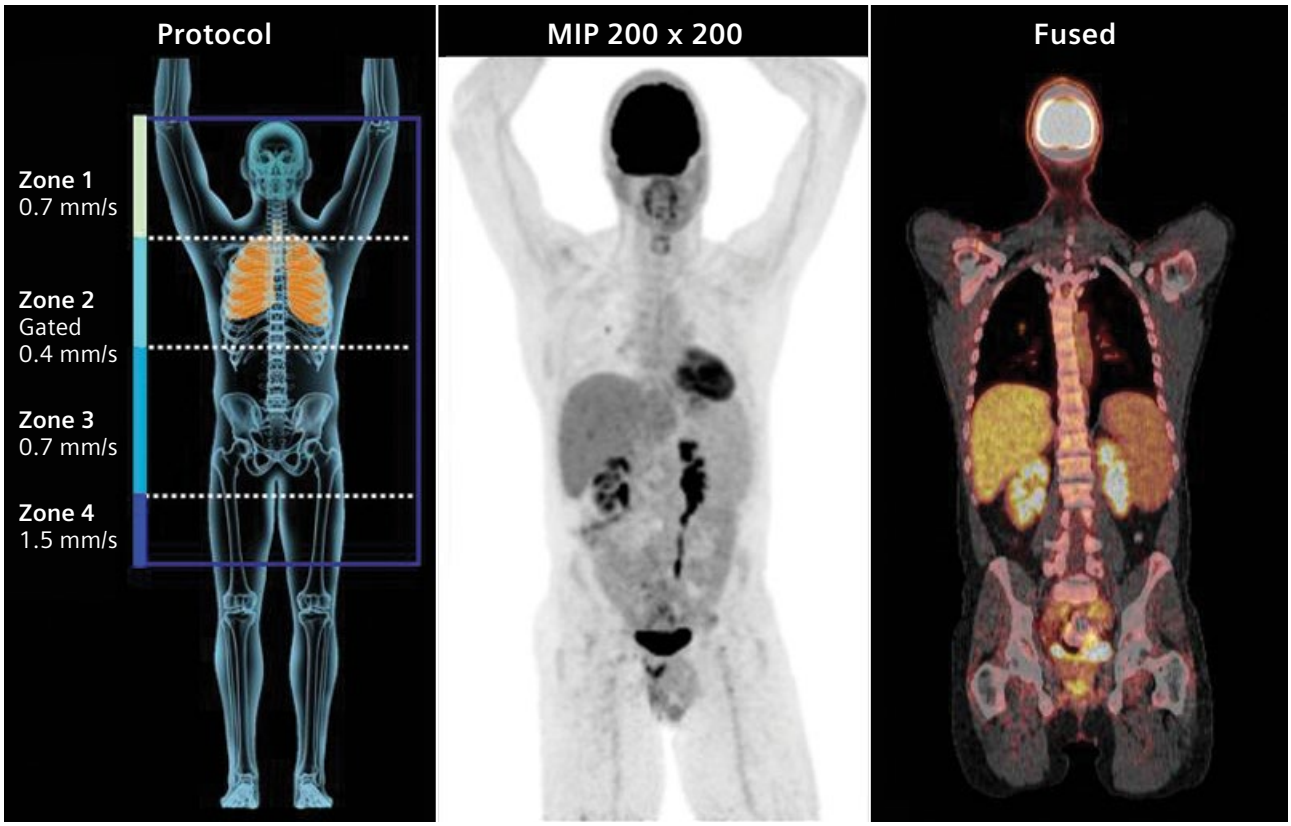


Figure 1: Whole-body PET images acquired with FlowMotion show a solitary lung nodule.

Comments

This clinical example illustrated the improved visualization and higher quantitative accuracy for small lung nodules that are achieved through amplitude-based, optimized respiratory gating (HD•Chest), which eliminates respiratory motion-related peripheral blurring and loss of lesion conspicuity. The 23% higher SUV_{max} obtained with HD•Chest—secondary to elimination of respiratory motion-related partial volume effects and blurring—strongly supported the diagnosis of malignancy in the lung nodule. Although the SUV_{max} of 2.97 obtained from the non-gated study suggests malignancy, the increased SUV_{max} following elimination of respiratory motion-related effects imparted significant additional diagnostic confidence and also confirmed the absence

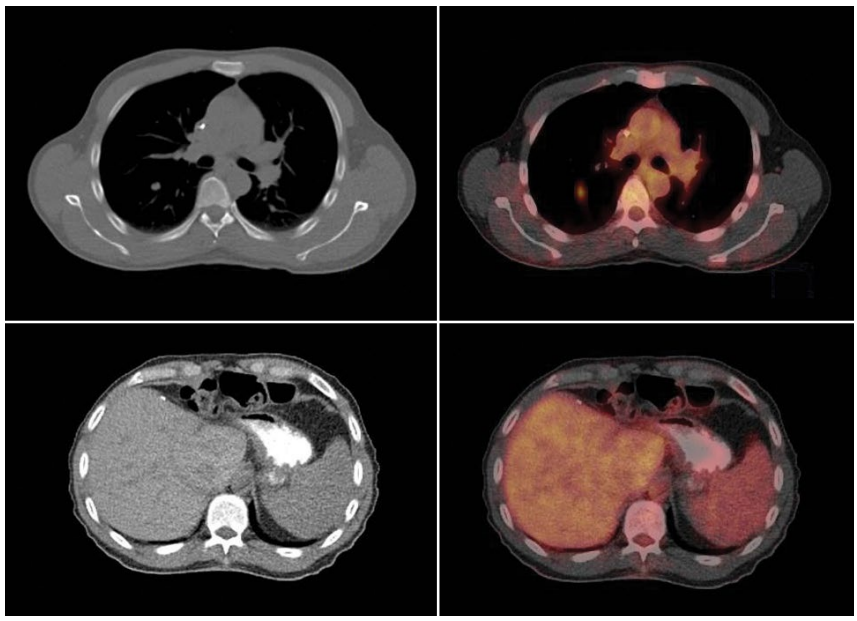


Figure 2: CT and fused PET/CT images show a solitary hypermetabolic lung nodule and normal tracer uptake in the resection bed in the anterior part of the left lobe of the liver.

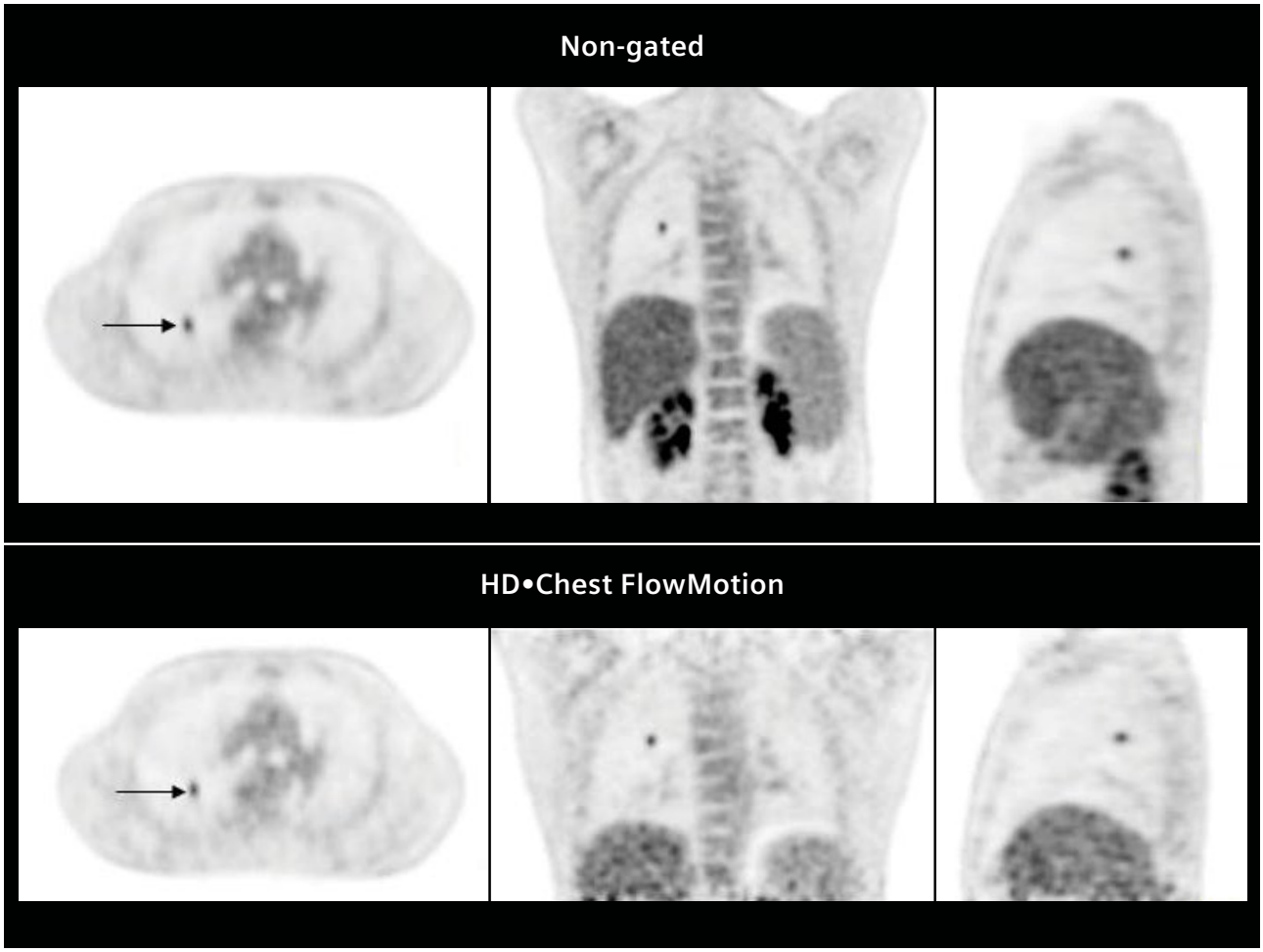


Figure 3: Comparison of thoracic non-gated PET and HD•Chest reconstructions of the thorax showing sharper delineation of hypermetabolic solitary lung nodule with HD•Chest (*arrow*).

of other lung lesions. CT showed the lung nodule to be 8 mm in diameter. The sharp delineation of such a small nodule with HD•Chest reflects the improved lesion conspicuity, target-to-background ratio and higher quantitative accuracy obtained through the elimination of respiratory motion-related blurring and partial volume effects with HD•Chest.

Although respiratory gating helps eliminate respiratory motion and is able to sharply define the lesion in individually gated frames, the relatively lower count statistics and higher background noise in the individual frames may hinder visualization of very small lesions or lesions with low uptake. HD•Chest uses amplitude-based gating, which uses a portion of the total gated list-mode data with the least motion based on amplitude histogram. This provides relatively motion-free images with higher count statistics for higher image quality and improved small lesion conspicuity. FlowMotion acquisition enables respiratory gating within extremely flexible ranges, which helps generate motion-managed HD•Chest reconstructions precisely from the regions of interest without undue time penalty.

Conclusion

Accurate SUV quantification is key to management decision-making in lung nodules. SUV_{max} higher than 2.5 has been shown to have a higher probability of malignancy. Since SUV in lung nodules may be affected by partial volume effects, due to respiratory motion in non-gated PET, motion management in PET acquisition, like HD•Chest, may improve quantification due to elimination of respiratory motion effects. This is particularly important for small nodules with lower levels of hypermetabolism as seen in early lesions. Detection of small nodules with low uptake may also be enhanced by HD•Chest since

lesion conspicuity is improved by eliminating respiratory motion-related blurring. Integration of HD•Chest with FlowMotion acquisition offers great flexibility of the area to be covered and opens the possibility of seamless routine use of this technique, with potential improvement in lesion detectability and informed therapy decision. Thus, FlowMotion enables gated acquisition in narrow or wide ranges not limited by bed positions in order to perform acquisition tailored to the patient's clinical requirements. ■

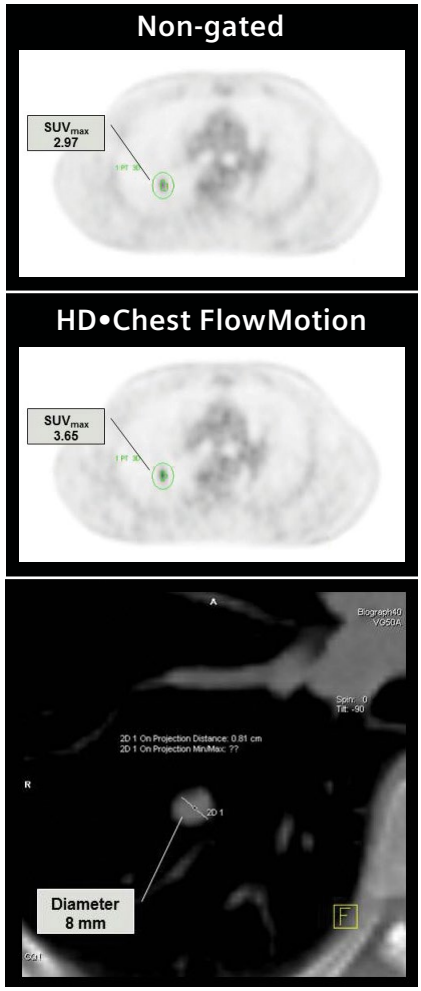


Figure 4: CT shows a solitary lung nodule with a diameter of 8 mm. HD•Chest shows higher SUV_{max} of 3.65 of the lung nodule compared to SUV_{max} of 2.97 obtained from non-gated PET acquisition of the lung.

Examination Protocol

Scanner: Biograph mCT Flow

PET	
Injected dose	334 MBq (9.027 mCi) ^{18}F-FDG
Scan delay	60 min
Acquisition	Variable table speed (*Figure 1*) ultraHD•PET with integrated respiratory gating for thorax and upper abdomen
CT	
Tube voltage	100 kV
Tube current	45 mAs
Slice thickness	5 mm

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

** Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

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Case 3

Improved Visualization of Small Liver Metastases Using HD•Chest and FlowMotion

By Partha Ghosh, MD, Molecular Imaging Business Unit, Siemens Healthcare

Data courtesy of Royal Brisbane Hospital, Brisbane, Australia

History
An 81-year-old male patient with a history of colorectal carcinoma treated with partial colectomy presented with elevated serum carcinoembryonic antigen (CEA). In view of the suspicion of metastases, the patient was referred for a PET/CT scan.

PET/CT studies were performed on a Biograph mCT Flow™* scanner. After the non-contrast, whole-body CT, a whole-body PET acquisition was initiated using variable table speed. The liver and upper abdomen were acquired with integrated respiratory gating. Faster acquisition was used for the extremities, in order to optimize acquisition time.

The whole-body PET study was reconstructed as a non-gated, 200 x 200 matrix reconstruction. However, the region of the liver and upper abdomen was reconstructed with a higher matrix (400 x 400) as a non-gated study. The gated data for the same region was also reconstructed as HD•Chest with 50% duty cycle in order to obtain relatively motion-free images of the liver for improved evaluation of liver metastases. FlowMotion™ acquisition enabled routine use of HD•Chest as a part of seamless routine acquisition with high flexibility of the range of the region of respiratory gated acquisition.

Diagnosis
Coronal maximum intensity projection (MIP) and thin MIP images of the whole-body PET study show two focal hypermetabolic lesions in the liver, which suggested liver metastases. Glucose-avid region in the left lung and another small focal region in right lung are probably related to inflammation. Left renal pelvis shows tracer retention. Note the linear uptake and blurring of the margins of the small liver lesions, which was related to respiratory motion during acquisition since the whole-body study is reconstructed as a non-gated acquisition.

CT and fused PET/CT images of the thorax showed honeycombing of the left lung and right lung base, which corresponded to high tracer uptake and suggested extensive bilateral inflammatory lesions, probably resolving pneumonitis.

** Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

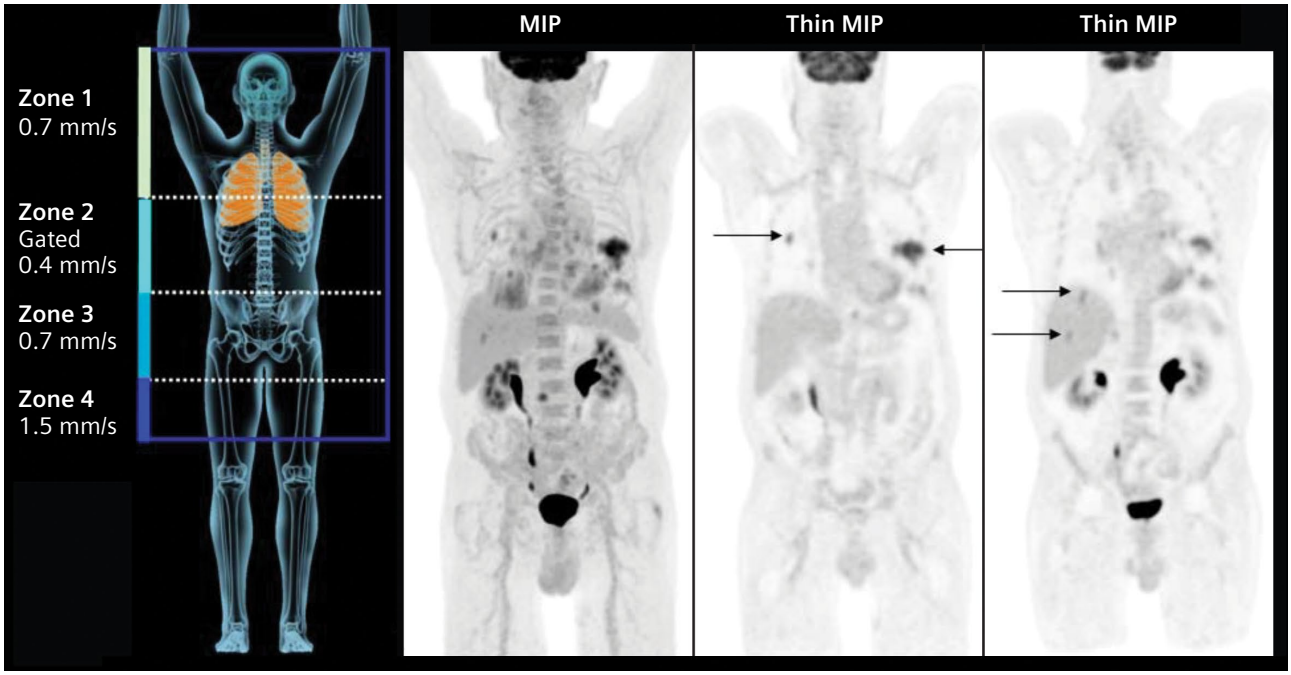

Figure 1: Whole-body PET images acquired with FlowMotion show lung and liver lesions.

The high-resolution, non-gated reconstruction of the respiratory-gated acquisition of the upper abdomen showed the liver metastases as small elongated focal hypermetabolic areas. The elongated nature of the uptake and blurring of the edges secondary to respiratory motion were especially prominent in the liver lesion near the dome of the diaphragm.

The HD•Chest reconstruction of the respiratory-gated data of the liver and upper abdomen demonstrated improved delineation of both the liver metastases with higher lesion conspicuity, increased target-to-background with improved visibility and

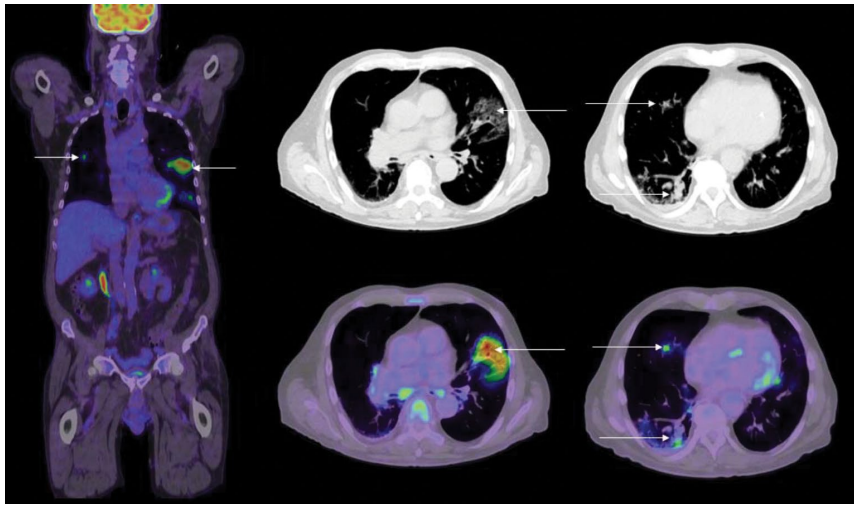

Figure 2: CT and fused PET/CT images suggest the lung lesions to be of inflammatory origin.

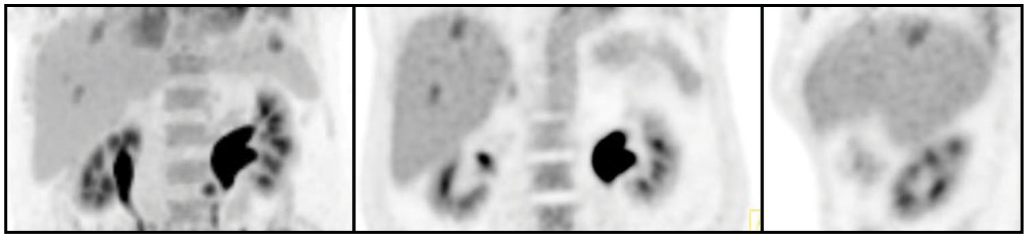

Figure 3: 200 x 200 matrix reconstruction of non-gated PET acquisition of liver and upper abdomen shows two liver lesions with blurring due to respiratory motion.

sharper definition of the edges, as compared to non-gated acquisition. This was especially conspicuous in the lesion near the dome of the diaphragm.

Quantitative comparison between non-gated reconstruction and HD•Chest showed a substantially higher SUV_{max} with HD•Chest compared to that obtained from the non-gated reconstruction. SUV_{max} went from 3.92 to 4.8 with HD•Chest, an increase of 22%, which can be attributed to the lack of peripheral blurring and smaller lesion dimension achieved with HD•Chest by eliminating the respiratory motion effects. FlowMotion technology enables respiratory-gated acquisition in flexible ranges as was utilized in this patient who required gating for the liver but not the lung in view of the predominance of liver metastases in colorectal carcinoma.

Comments

This clinical example illustrates the significant distortion of small liver lesions with peripheral blurring and loss of conspicuity secondary to respiratory motion when PET is acquired without respiratory gating. This may lead to lower detectability of small liver metastases with PET/CT.

Although respiratory gating helps eliminate respiratory motion and is able to sharply define the lesion in individual gated frames, the relatively lower count statistics and higher background noise in the individual frames may hinder visualization of very small lesions or lesions with low uptake.

HD•Chest uses amplitude-based gating, which utilizes the portion of the total gated list mode data that has the least motion based on amplitude histogram and provides relatively motion-free images with higher count statistics for improved image quality and small lesion conspicuity.

HD•Chest is an attractive tool for improved delineation of small liver lesions, since it provides relatively motion-free images with sufficient image quality and count density without significant increase in scan time. HD•Chest, when integrated into FlowMotion acquisition, can be used with extreme flexibility, thereby enabling precise definition of the region to be acquired with respiratory gating.

In a recent study comparing non-gated PET and HD•Chest in 31 patients with liver metastases,1 out of a total of 82 hepatic and 25 perihepatic lesions, 13 new lesions were identified by HD•Chest as compared to standard PET. In this study, five-minute optimal gating (HD•Chest) acquisition demonstrated improved image quality and 66% higher target to background ratio and 24% higher SUV_{max} for metastatic lesions as compared to non-gated PET acquired at 2.5 minutes per bed. In a patient with a single lesion seen on standard PET, the use of HD•Chest identified two liver metastases, which significantly changed patient management from surgical removal of solitary metastases to radiofrequency ablation of two metastatic lesions. In another patient, HD•Chest helped the physician identify a lesion in the pancreas that had been previously identified as a peritoneal metastases by non-gated PET.

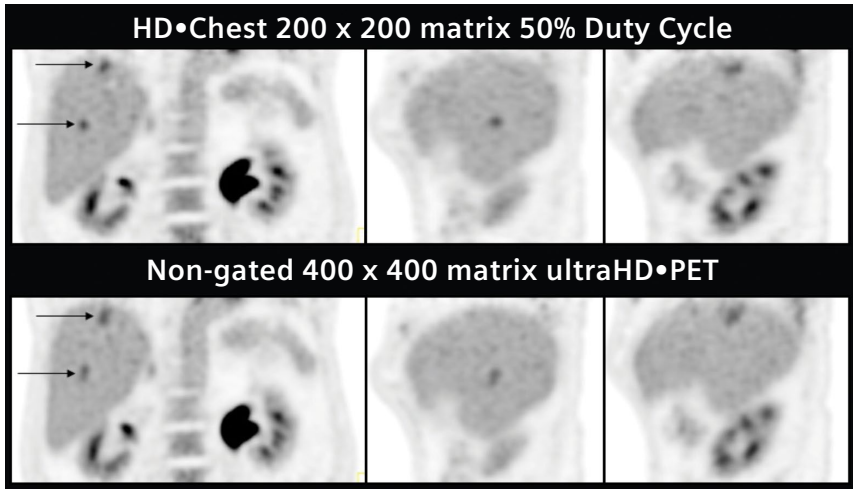

Figure 4: Comparison of non-gated and HD•Chest reconstructions of the liver and upper abdomen shows improved definition of liver lesions when using HD•Chest.

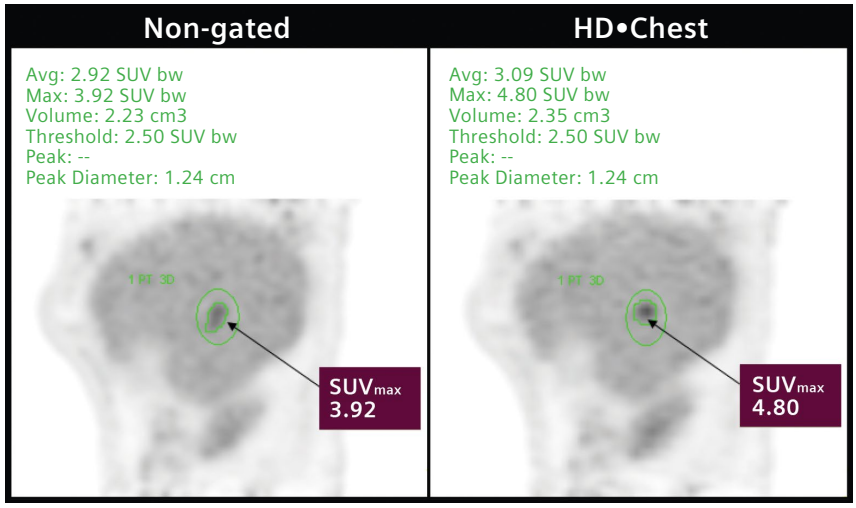

Figure 5: Comparison of SUV_{max} of liver lesion shows significantly higher SUV_{max} with HD•Chest than in the non-gated acquisition.

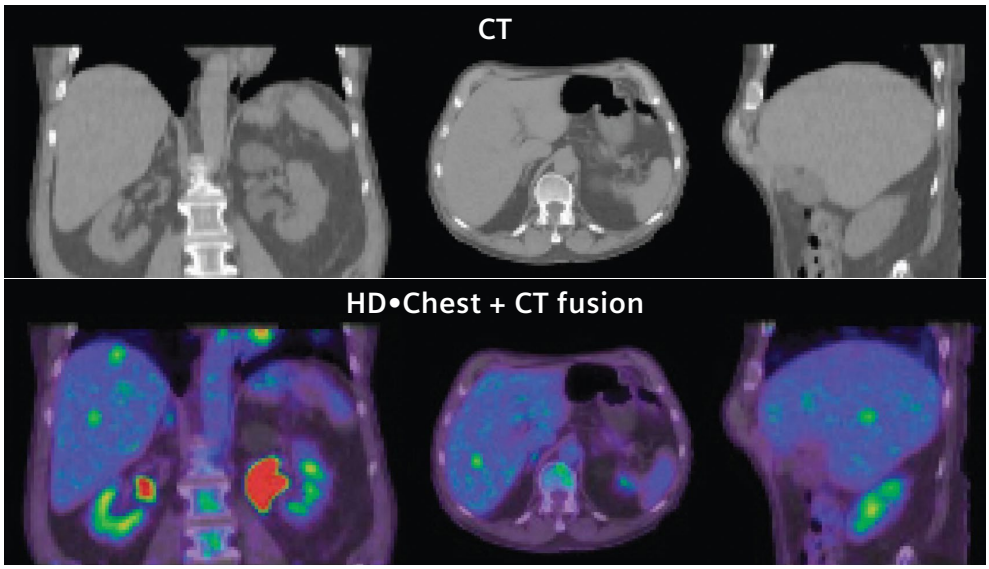

Figure 6: Non-contrast CT and fusion of CT and HD•Chest reconstruction shows sharp boundaries of small liver metastases that are not well visualized on non-contrast CT, thereby highlighting the value of PET and elimination of respiratory motion for delineation of such small lesions with minimal morphological changes.

Conclusion

In view of the therapy options, such as surgical removal of solitary liver metastases, cryotherapy, radiofrequency ablation of individual lesions or chemotherapy in extensive metastases, proper detection of early liver metastases or exclusion of liver lesions assumes a key importance in the therapy decision. Thus, integrated techniques like HD•Chest, which improve the diagnostic confidence and detectability of small liver, lung or upper abdominal lesions without undue time burden, are of value in PET/CT scanning.

Continuous bed motion and anatomy-based planning with FlowMotion opens the possibility of seamless, routine use of HD•Chest with the opportunity for improvement in lesion detectability and more informed therapy decisions. ■

Examination Protocol

Scanner: Biograph mCT Flow

PET	
Injected dose	334 MBq (9.027 mCi) ^{18}F-FDG**
Scan delay	60 min post injection
Protocol	FlowMotion acquisition, variable table speed. (*Figure 1*) ultraHD•PET with integrated respiratory gating for upper abdomen
CT	
Tube voltage	120 kV
Tube current	56 eff mAs
Slice thickness	3 mm

References:
[1] Van Der Gucht, et al. (2013). European Journal of Radiology, Nov. 2013 online, article in press.

* Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

** Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

The statements by Siemens customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that other customers will achieve the same results.

Case 4

Sharper Delineation of Small Pulmonary Metastases with HD•Chest in a Patient with Breast Carcinoma

By Dustin Osborne, PhD

Data courtesy of the University of Tennessee Medical Center, Knoxville, Tenn., USA

History

A 65-year-old woman with a history of breast carcinoma was initially treated with lumpectomy and local radiation therapy. With evidence of a lung nodule from a chest X-ray, the patient presented for a follow-up. Due to the possibility of metastases, the patient was referred for Fludeoxyglucose F 18 (^{18}F-FDG)* PET/CT.

An ^{18}F-FDG PET/CT study was performed 90 minutes following an IV injection of 11 mCi of ^{18}F-FDG. Variable table speed FlowMotion™ acquisition was performed on a Biograph mCT Flow™** system with incorporation of respiratory gating in the region comprising of the lungs and the upper part of the liver. This was acquired with a slow table speed (0.5 mm/sec) with integrated respiratory gating for this extended range. The region of the head and neck was scanned at a standard table speed (1 mm/sec), while the pelvis and extremities were scanned with faster table speeds (1.5 mm/sec) for optimized acquisition time. The gated thoracic and abdominal region was reconstructed with HD•Chest for motion-frozen images and improved lesion detectability. Whole-body, non-gated images at 200 x 200 matrix were also reconstructed from the variable table speed acquisition. (The table speeds and ranges are demonstrated in *Figure 1*.)

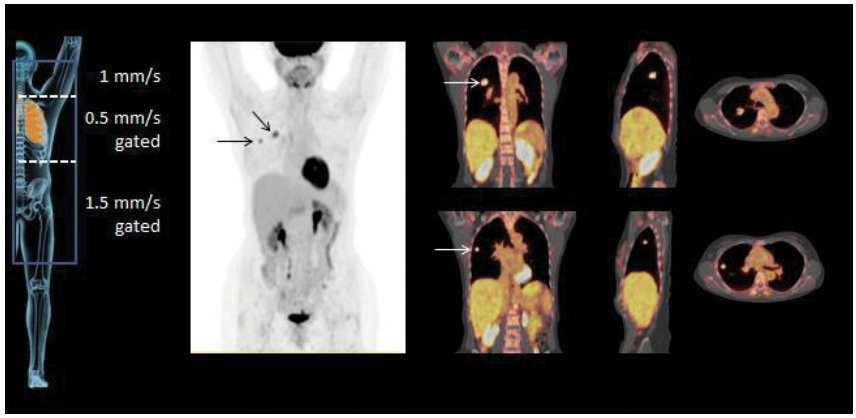

Figure 1: Whole-body PET/CT study demonstrates two hypermetabolic lung nodules.

Diagnosis

Figure 1 shows a non-gated 200 x 200 matrix reconstruction of the whole-body PET/CT that was acquired with variable table speeds. Two hypermetabolic metastatic lung nodules were visualized in

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

the right upper lobe. No other distant metastases were visualized.

The HD•Chest images, reconstructed with 33% of the gated list mode data and with low respiratory motion, showed, in comparison to non-gated PET, sharper delineation and higher lesion-to-background contrast of a small 8 mm hypermetabolic lung nodule (*Figure 2, arrows*), due to elimination of respiratory motion-related blurring by HD•Chest. In the non-gated reconstruction, this small nodule was not well visualized in the PET MIP images (*Figure 1*) and was poorly delineated with low ^{18}F-FDG uptake in the fused PET/CT images and the PET MPR slices (*Figure 2*).

Comments

Improved visualization of such small lesions with motion management—provided by respiratory gating and HD•Chest reconstruction—increases diagnostic confidence in the detection of lung metastases in cancers such as breast, bladder, thyroid and colorectal tumors. In this particular clinical case, improved detection of additional small lung metastases did not necessarily result in a major change in the therapy decision due to the presence of two larger lung metastases. In such situations, aggressive chemotherapy is generally the therapy of choice, since ablation of individual lung metastases is ruled out because of the presence of multiple lesions. Improved localization of a small right, lower-lung-base metastasis did however highlight the disseminated spread of microscopic metastases and the potential for appearance of new lesions. Aggressive chemotherapy also aims to reduce the metastatic burden and slow the appearance of new lesions, which is also advantageous in this case. Since chemotherapy is associated with systemic effects, and ablation of solitary or multiple small lung or liver lesions is a therapy option, improved lesion detectability offered by HD•Chest motion management is helpful for patient management decisions.

Conclusion

Flexible range of respiratory gating, made possible with variable table speed FlowMotion acquisition, imparts the ability to perform gating on limited or extended regions without undue time penalty. HD•Chest reconstructions obtained from gated list mode data provide relatively motion-frozen images. This improves the detectability and SUV quantification of small lesions subject to significant respiratory motion and related blurring as well as partial volume effects, as demonstrated in this clinical example. ■

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

** Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

The statements by Siemens customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that other customers will achieve the same results.

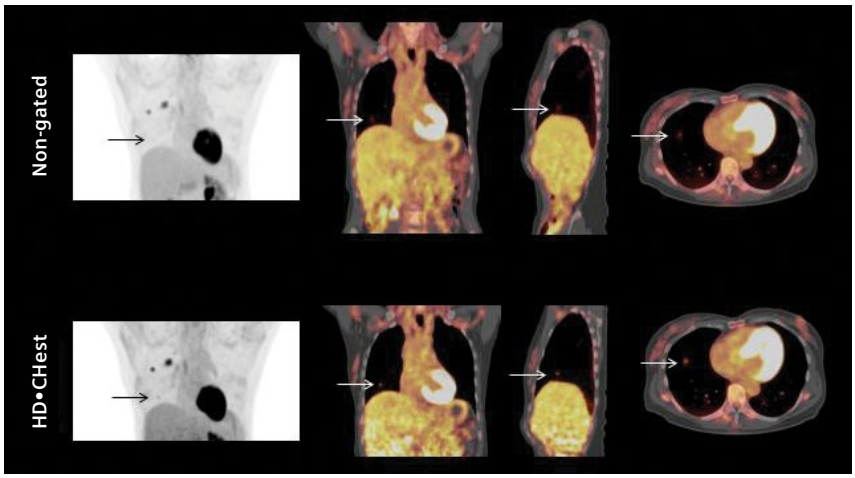

Figure 2: Comparison of MIP and fused PET/CT images of HD•Chest and non-gated reconstructions of the thorax shows improved delineation of a small nodular metastatic lesion in the lower-right lung with HD•Chest (*arrow*).

Examination Protocol

Scanner: Biograph mCT Flow

PET	
Injected dose	11 mCi (407 MBq) ^{18}F-FDG
Scan delay	90 min post injection
Acquisition	Zone 1, 1 mm/sec; Zone 2, 0.5 mm/sec gated; Zone 3, 1.5 mm/sec

CT	Whole-body scan mode
Tube voltage	120 kV
Tube current	152 eff mAs
Slice collimation	64x0.6 mm
Slice thickness	5 mm
CTDIvol	11.63 mGy

Case 5

Improved Visualization of Focal Lymphomatous Deposit in Gastric Wall using ^{18}F-FDG* PET/CT and HD•Chest

By Dustin Osborne, PhD

Data courtesy of the University of Tennessee Medical Center, Knoxville, Tenn., USA

History
A 55-year-old man with a long-standing history of gastritis presented with a single episode of profuse vomiting that contained blood stains. A gastric endoscopy demonstrated an area of thickening of rugae and inflammation in the mucosa of the gastric fundus. A histopathology from the biopsy sample from that mucosal segment showed gastric mucosa-associated lymphoid tissue (MALT) lymphoma. The patient was referred for a Fludeoxyglucose F 18 (^{18}F-FDG) PET/CT to evaluate the extent of the tumor as well as extra gastric spread or other nodal involvement.

The study was performed on a Biograph mCT Flow™** system using continuous bed motion (FlowMotion™) acquisition, a technique that enables flexible range acquisitions with variable table speeds and, depending on the organ or region of interest, the ability to incorporate respiratory gating for any range. Because respiratory motion can affect the gastric lesional uptake and the perigastric region, a respiratory-gated acquisition was performed on the thorax and abdomen as part of the FlowMotion acquisition. Amplitude-based gated images were obtained with HD•Chest, using 33% of the list mode respiratory-gated data to obtain relatively motion-frozen images for improved delineation of lesions subjected to respiratory motion-induced blurring.

Diagnosis
HD•Chest images showed a small focal area of increased uptake in the gastric mucosa at the region of the gastric fundus (*Figure 1, cross-hairs*). The non-gated images did not show significantly higher uptake within the lesion when compared to the rest of the gastric mucosa. However, the HD•Chest images showed higher lesion contrast with the elimination of respiratory motion-related blurring. This made visualization of the small solitary gastric lesion possible. There are no other hypermetabolic lesions in the gastric mucosa, the perigastric region or the locoregional lymph nodes, suggesting that the patient had a small solitary MALT gastric lymphoma with an indolent course and good prognosis.

Comments
Although MALT lymphomas are uncommon, they frequently involve the stomach mucosa. ^{18}F-FDG PET/CT has shown lower detection rates for MALT lymphomas in the stomach (62%) when compared to those in the bronchus (94%) or the head and neck (90%).[1] Although MALT lymphomas are ^{18}F- FDG avid, the lower sensitivity of PET/CT for gastric lym-

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

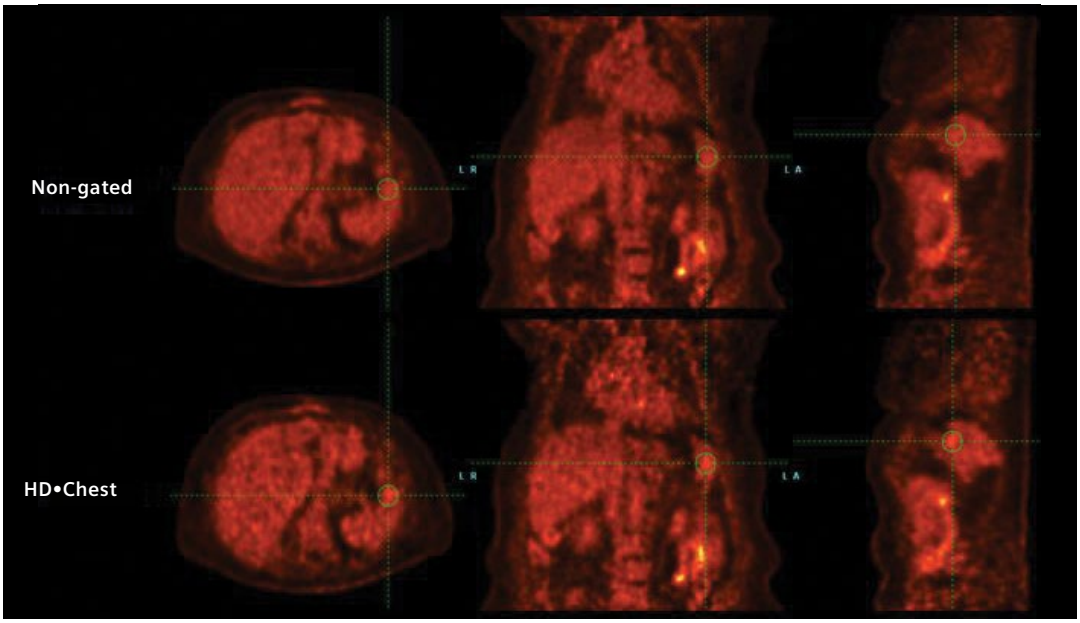

Figure 1: omparison of non-gated PET and HD•Chest images of the thorax and upper abdomen demonstrates improved visualization of the small focal area of increased uptake in the gastric mucosa.

phoma may be related to a smaller initial size, lower uptake and motion. Elimination of respiratory motion using HD•Chest improves detection of small gastric lesions as in the present case.

The standard uptake value (SUV) of MALT lymphomas have shown to correlate significantly with pathological malignant potentials, with high-grade MALT lymphomas demonstrating higher SUV.[2] Since HD•Chest improves the accuracy of SUV calculation in a small lesion by eliminating respiratory motion-related blurring, this technique can improve characterization of such lesions and help differentiate low grade indolent lesions from more aggressive ones. SUV_{max} has helped differentiate gastric MALT lymphomas from gastric carcinoma, which demonstrated higher values, although both conditions showed similar gastrointestinal wall thickness on CT.[3] A high SUV in the baseline ^{18}F-FDG PET/CT, and a lower reduction in the SUV within three months after H.Pylori eradication therapy, has shown to be associated with treatment-failure in H. Pylori-positive, low-grade gastric MALT lymphoma patients who are undergoing eradication treatment.[4] These studies indicate the importance of SUV accuracy and higher detectability for initial staging, characterization, prognostication and therapy follow-up.

Conclusion

HD•Chest helps improve lesion detectability by eliminating respiratory motion-related blurring and quantitative accuracy of SUV. Integration of respiratory gating and HD•Chest in flexible ranges, which is made possible by FlowMotion acquisition, provides a seamless workflow and can be used routinely in patient imaging. As a result, a large range of patients, especially those with suspected liver, gastric or pancreatic lesions, could receive improved accuracy in PET imaging. ■

Examination Protocol

Scanner: Biograph mCT Flow 64

PET	
Injected dose	11 mCi (407 MBq) ^{18}F-FDG
Scan delay	90 min post injection
CT	Whole-body scan mode
Tube voltage	120 kV
Tube current	141 eff mAs
Slice collimation	64x0.6 mm
Slice thickness	5 mm

References:
[1] Treglia et al. Hematol Oncol. 2014.
[2] Watanabe et al. Int. J. Hematol. 2013. 97(1): 43-49.
[3] Fu et al. PLoS ONE. 2012. 7(12): e50914.
[4] Song et al. Gut Liver. 2011; 5: 308-31.

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

** Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

Case 6

Detection of Brain Metastases in a Patient Operated Neuroendocrine Tumor with ^{68}Ga DOTATATE* PET/CT

By Frank Bengel, MD

Data courtesy of Medical University of Hannover, Hannover, Germany

History

A 59-year-old man with a history of a high-grade neuroendocrine tumor (carcinoid) in the intestine with metastases in the right lobe of the liver, who had been treated with intestinal resection and right hemihepatectomy, presented with rising serum chromogranin A levels. This was suspicious for tumor recurrence. As such, the patient was referred for ^{68}Ga DOTATATE PET/CT for the detection of a potential recurrent neuroendocrine tumor.

The PET/CT study was performed 1 hour after an intravenous injection of 150 MBq of ^{68}Ga DOTATATE. The study was performed on Biograph mCT Flow™**, using continuous bed motion (FlowMotion™) acquisition and a uniform table speed of 0.7 mm/sec following a low-dose CT for attenuation correction. A whole-body PET/CT study was reconstructed with a standard matrix of 200 x 200. The brain was separately reconstructed with a higher matrix of 400 x 400, in order to obtain a sharper definition of cerebral lesions.

Diagnosis

^{68}Ga DOTATATE PET/CT showed multiple focal areas of increased uptake in the brain, which suggested cerebral metastases (*Figure 1*). There

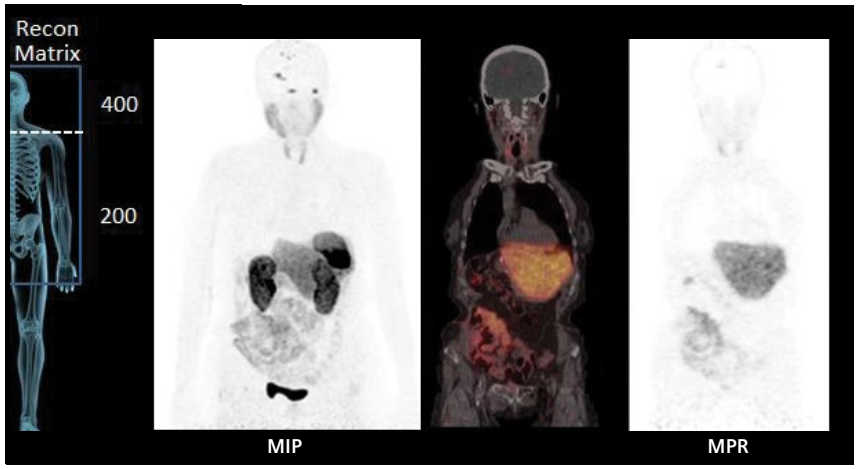

Figure 1: Whole-body 200 x 200 matrix reconstructions of ^{68}Ga DOTATATE PET/CT and fused images show multiple focal uptakes in the brain, which suggests metastases.

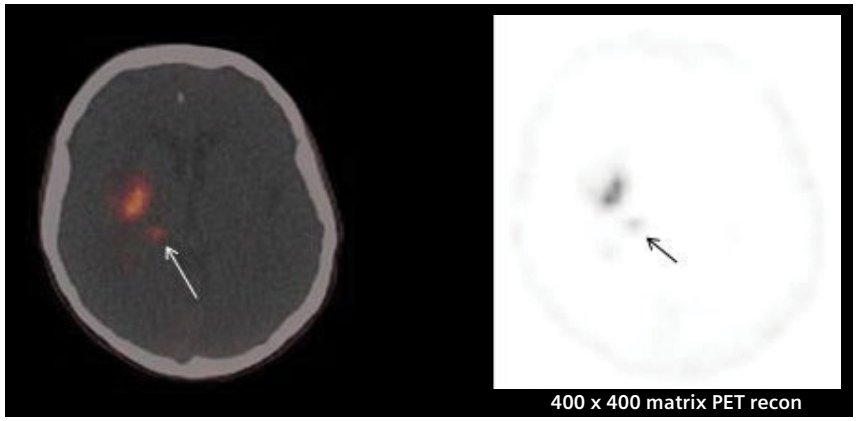

Figure 2: Hi-Rez 400 x 400 matrix PET recon of the brain and fused images show multiple focal areas of tracer uptake in the right parietal cortex and basal ganglial region.

* ^{68}Ga DOTATATE and ^{177}Lu DOTATATE referenced herein are not currently recognized by the US FDA as being safe and effective, and Siemens does not make any claims regarding their use.

were no other well-defined focal lesions in the body that suggested metastases. The remaining part of the liver (left lobe, post right hemi-hepatectomy status) was enlarged secondary to hypertrophy as expected, with uniform and normal tracer uptake. The spleen, kidneys, salivary glands and thyroid showed normal tracer uptake, as per the physiological distribution of ^{68}Ga DOTATATE. There was a considerable amount of tracer uptake in the small bowel, but without any focal abnormal area of uptake.

400 x 400 matrix reconstructions of ^{68}Ga DOTATATE PET/CT (*Figure 2*) showed multiple focal areas of increased uptake in the brain parenchyma, which suggested functioning neuroendocrine tumor metastases. Hi-Rez PET reconstructions delineated small brain metastases (*arrows*) due to a lower partial volume effect. High count statistics obtained by a slower continuous bed motion acquisition with a bed travel speed of 0.7 mm/sec were the key to achieving high image quality and lesion contrast, even with a higher matrix reconstruction with a smaller voxel size.

Because functioning brain metastases were detected with avid ^{68}Ga DOTATATE uptake, peptide receptor radionuclide therapy (PRRT) with ^{177}Lu DOTATATE* was considered as part of the approach for managing the metastatic brain lesions.

Comments

PET/CT using ^{68}Ga-labeled somatostatin analogs has been used in neuroendocrine tumors that overexpress somatostatin receptors. Approximately half of patients have metastatic disease at presentation, and early, accurate diagnosis and staging are crucial for therapy decisions. One of the main advantages of PET/CT is the possibility of quantifying tracer uptake, which reflects receptor density of the tumor and thus facilitates personalized diagnosis and therapy.

Similar to ^{68}Ga DOTATOC or DOTATATE, PET/CT with ^{68}Ga somatostatin analogs have demonstrated high impact on patient management in several studies. These studies have shown that a course of treatment had changed in 50%-60% of cases because of PET/CT results.[1] A meta-analysis of 16 clinical studies, involving 567 patients with suspected thoracic or gastroenteropancreatic NETs,[2] found pooled sensitivity and specificity of PET/CT with ^{68}Ga somatostatin analogs to be 93% and 91%, respectively, for detection of primary or metastatic NETs. In such patients, the analysis recommends that ^{68}Ga somatostatin analogs be considered as a first-line diagnostic imaging method. Analogs like ^{68}Ga DOTATOC, ^{68}Ga DOTATATE and ^{68}Ga DOTANOC are extensively used in clinical studies demonstrating fast pharmacokinetics, target localization, blood clearance and renal excretion—all with comparable sensitivity and accuracy.[3]

Individualized therapy planning with adjustment of injected radioactivity dose during PRRT of NETs is necessary because of high inter-patient variability in healthy organ uptake.[4] Accurate quantification of tumor uptake with ^{68}Ga DOTATATE PET/CT has a major impact in dosimetry for ^{177}Lu DOTATATE therapy. A major impact of PET/CT with ^{68}Ga somatostatin analogs is related to the detection of additional or unknown metastases. In comparison, SPECT- or CT-only studies often lead to just a change in management. In a study by Gabriel[5] involving 84 patients with suspected NETs, ^{68}Ga DOTATOC PET/CT identified lesions that were not defined on CT in 21.4% of patients. Gabriel's study primarily relates to small bone and liver metastases. The present case also illustrates the ability of ^{68}Ga DOTATATE PET/CT to detect functioning metastases from NET, especially small brain metastases, which are better detected with higher matrix PET reconstruction.

Conclusion

Higher matrix reconstruction of PET data improves the target-to-background ratio of small lesions, thereby improving lesion conspicuity. Higher matrix reconstruction requires higher count statistics to decrease noise. FlowMotion technology offers acquisition of flexible ranges with variable table speeds, which enables slower acquisition with higher count statistics in regions requiring higher matrix reconstruction for increased small lesion detectability. The present case was acquired with uniform, but slower table speeds for high image quality and increased count statistics in that region in order to subsequently provide any relevant acquisition range with higher matrix reconstruction. ■

Examination Protocol

Scanner: Biograph mCT Flow

PET	
Injected dose	150 MBq (4.054 mCi) ^{68}Ga DOTATATE
Scan delay	60 min post injection
Acquisition	Zone 1, 0.7 mm/sec
CT	Whole-body scan mode
Tube voltage	120 kV
Tube current	48 eff mAs
Slice collimation	32 x 1.2 mm
Slice thickness	5 mm

References:
[1] Frilling et al. Ann Surg. 2010, 252: 850-856.
[2] Treglia et al. Endocrine. 2012, 42: 80-87.
[3] Velikyan et al. J Nucl Med. 2014, 55: 204-210.
[4] Sandstrom et al. J Nucl Med. 2013, 54: 33-41.
[5] Gabriel et al. J Nucl Med. 2007, 48: 508-518.

* ^{68}Ga DOTATATE and ^{177}Lu DOTATATE referenced herein are not currently recognized by the US FDA as being safe and effective, and Siemens does not make any claims regarding their use.

** Biograph mCT Flow is not commercially available in all countries. Due to regulatory reasons its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

Case 7

Follow-up PET/CT Detects Second Malignancy in Patient with Lung Carcinoma Treated by Radiation Therapy

By Samart Ratchadara, MD, and Ananya Ruangma, MD

Data courtesy of the Department of Nuclear Medicine, Wattanosoth Hospital, Bangkok, Thailand

History
A 66-year-old male presented with a history of a coughing, hemoptysis and evidence of a left hilar lung mass, which was seen on a chest X-ray and diagnosed as squamous cell carcinoma. The patient underwent Fludeoxyglucose F 18 (^{18}F-FDG)* PET/CT for initial staging. The study demonstrated a hypermetabolic left hilar mass without mediastinal or distant metastases. Therefore, the patient underwent radiation therapy for the lung mass, using 60 Gy delivered by 3D conformal radiation therapy at 2 Gy per fraction, 5 fractions per week. Six weeks after completing radiation therapy, the patient underwent a follow-up ^{18}F-FDG PET/CT.

The follow-up PET/CT was performed on Biograph mCT Flow™** 1 hour after an IV injection of 10 mCi (370 MBq) of ^{18}F-FDG. Following a whole-body contrast CT acquisition, PET was acquired using continuous bed motion (FlowMotion™ technology) at a uniform table speed of 1.0 mm/sec. The study was reconstructed using ultraHD•PET [Time-of-Flight (ToF) and point spread function (PSF)].

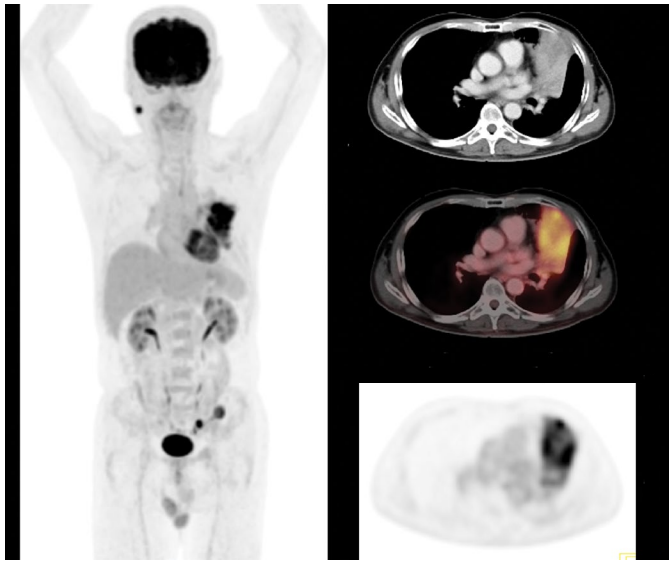

Figure 1: Post-radiation therapy PET/CT shows extensive inflammatory changes in the lung tumor bed in the left hilar region extending to the periphery anteriorly, which is typical of inflammatory infiltrate involving the affected lung lobe in the radiation field. No mediastinal or distal metastatic lesions are visible.

Diagnosis
Demonstrated in Figures 1-2, the post-radiation therapy follow-up PET/CT showed a large area of radiation-induced inflammatory changes leading to lobar consolidation and associated pneumonitis, which explained the CT findings of lobar opacity and hypermetabolism on PET.

Further review of the post-radiation therapy PET/CT revealed focal hypermetabolic lesions in the pelvic bowel, which were initially regarded as physiological uptake. However, careful review of the CT and fused PET/CT transverse slices at the level of the pelvic lesions demonstrated an eccentric mass lesion involving a region of the sigmoid colon, with corresponding hypermetabolism at the

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing info can be found on pages 54-56.

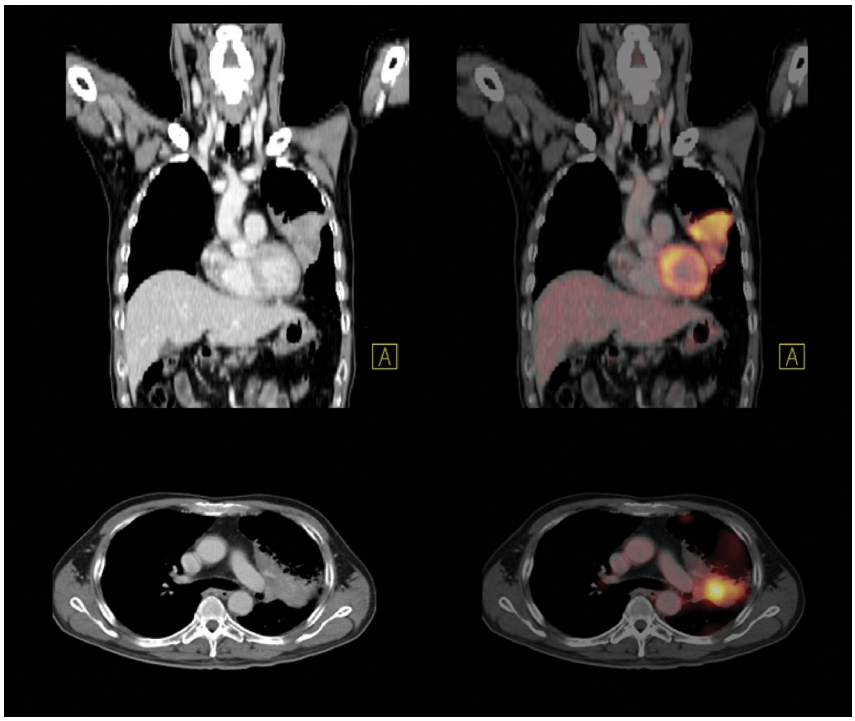

Figure 2: Contrast CT and fused PET/CT images show lobar consolidation with sharp delineation of lobar fissures and pneumonitis at the edges of the consolidation. Patchy hypermetabolism seen on fused PET/CT images reflect inflammation.

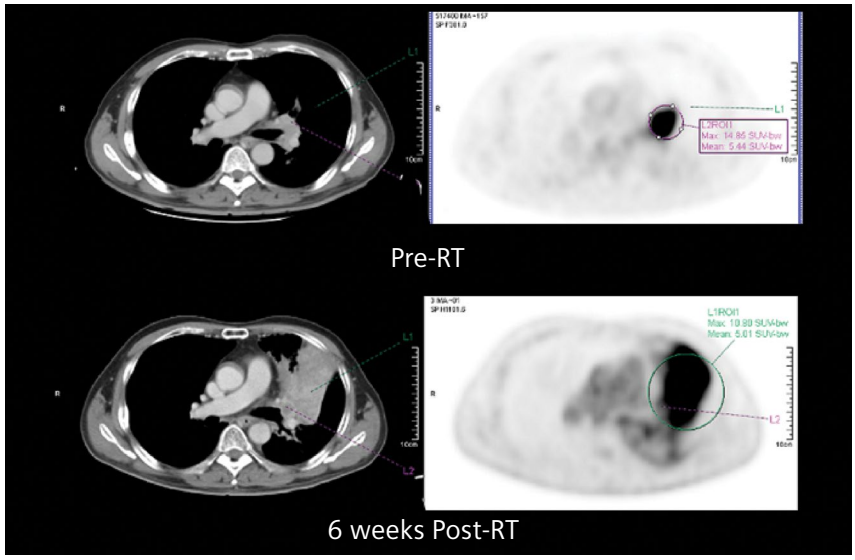

Figure 3: CT and PET transverse slices at the level of the left hilar tumor compared to pre- and post-radiation therapy (RT) PET/CT show a smaller hypermetabolic hilar mass in the pre-therapy PET (SUV_{max} 14.8), with a large area of consolidation and avid glucose uptake (SUV_{max} 10.8) involving the entire lobar segment seen in the post-therapy PET/CT, secondary to post-radiation inflammation. The comparison between the two scans and the uptake suggests resolution of the tumor with superimposition of the uptake related to the post-radiation inflammation.

tumor edge extruding into the colonic cavity (*Figure 4*). The other focal pelvic bowel hypermetabolism lateral to the sigmoid mass lesion appeared to be physiological uptake.

Based on the defined hypermetabolic mass lesion in the sigmoid colon, the pre-therapy PET/CT was reviewed to assess the colonic uptake initially and compare it to the follow-up PET/CT.

The focal bowel lesion was seen in the initial study, but was interpreted as physiological bowel uptake (*Figure 5*). The follow-up study, however, suggested a lesion suspicious for malignancy. A colonoscopy was performed, and a biopsy from the involved segment revealed an adenocarcinoma in the sigmoid colon (*Figure 6*).

Comments

This case illustrates the value of PET/CT for detecting second malignancy in patients with known cancer, and for assessment of tumor metabolism following standard conformal radiation therapy in lung carcinoma in which the inflammation-related hypermetabolism and consolidation may complicate interpretation of the lung tumor's post-radiation response.

Radiation pneumonitis is commonly visible 4 to 12 weeks following completion of radiation therapy involving the lung fields, although the extent of pneumonitis may vary among patients. In a study involving 24 patients with lung cancer who were treated with conformal radiation therapy (mean tumor dose = 55.8 Gy) and who underwent ^{18}F-FDG PET/CT 25-83 days (median = 59 days) post-therapy, PET/CT demonstrated significant radiation pneumonitis in 11 patients.[1]

There was a linear correlation between dose to normal lung and level of tracer uptake and SUV with predominant involvement of the volume of lung irradiated >20 Gy. The high tracer uptake related to radiation pneumonitis in the tumor bed may complicate visual and quantitative estimation of tumor response if post-radiation therapy PET/CT is performed following completion of radiation. In this context, studies have shown that PET/CT during the course of radiation therapy, particularly just after delivery of 40-45 Gy to the tumor, may be useful in accurate assessment of tumor response without excess radiation pneumonitis.[2]

A second primary tumor in this patient was detected due to the persistent focal hypermetabolism and eccentric sigmoid colon mass lesion defined by PET/CT and contrast CT. Although the focal hypermetabolism was visualized in the initial staging PET/CT, it was interpreted as physiological uptake in the absence of a significant mass lesion. Findings like these highlight the need for high-quality thin-slice CT with oral and intravenous contrast and good bowel preparation as part of a routine PET/CT study, even in situations where the abdomen is not the primary focus for the tumor or metastases.

Lung cancer is often associated with the presence or development of second primary cancer. In a study involving 860 patients with lung cancer, 44 patients subsequently developed second primary tumors.[3] Of the 44 patients, 31% were second lung

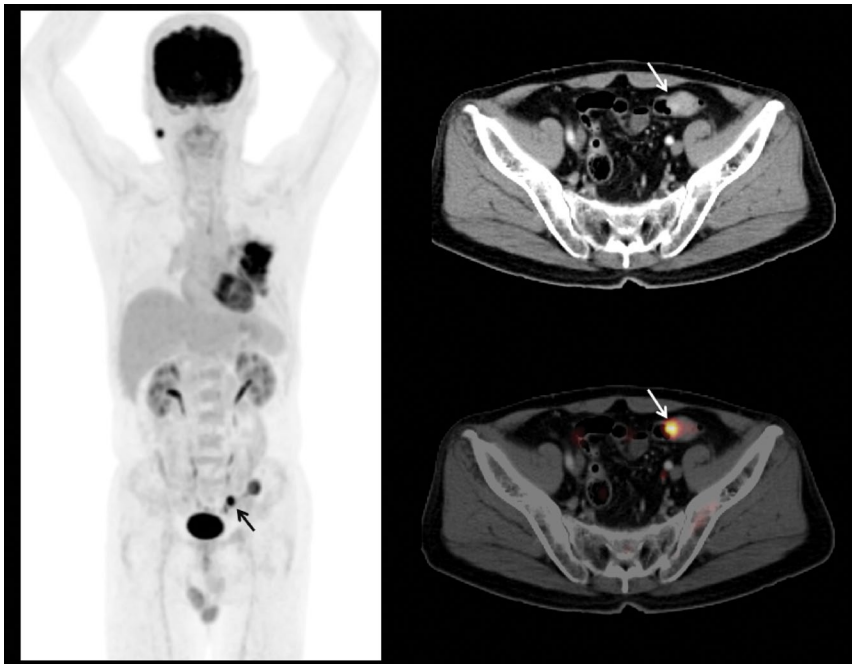

Figure 4: A focal hypermetabolic pelvic lesion (*arrow*) corresponds to eccentric mass encroaching into the cavity in the sigmoid colon, with maximum increase in uptake at the irregular tumor edge eroding into the colonic cavity. The appearance of the colonic mass and the associated hypermetabolism suggests a malignant colonic lesion rather than a benign polyp or physiological colonic uptake.

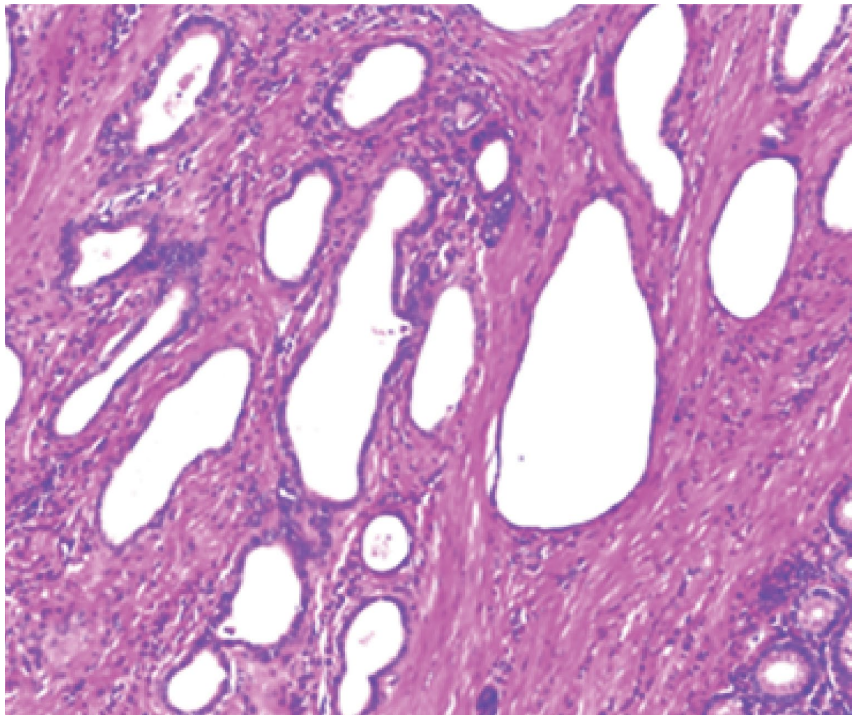

Figure 6: Histopathology of the tubulovillous adenoma in the sigmoid colon detected on PET/CT shows well-differentiated adenocarcinoma with high-grade dysplasia without lymphovascular or perineural invasion.

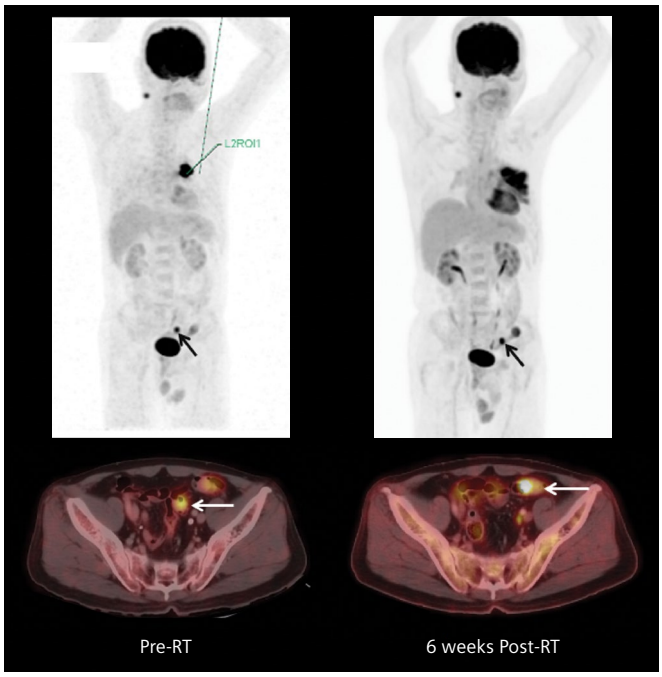

Figure 5: Comparison of PET maximum intensity projection (MIP) images of pre-therapy and 6 weeks post-radiation therapy PET/CT studies show a hypermetabolic primary lung tumor and the extensive radiation-induced inflammation in the tumor base and adjacent lung lobe. The PET images also show hypermetabolic focal colonic uptake in the initial study and in the follow-up study, and there is a slight increase in the degree of hypermetabolism assessed visually in the follow-up. The fused PET/CT images at the same level show a slight shift in the exact location of the affected bowel between the two studies, which is related to the extent of bowel luminal filling and bowel gas. The bowel lumen and associated hypermetabolism in the pre-therapy study was interpreted as physiological uptake since there was no clearly defined mass lesion. However, persistent hypermetabolism in the same colonic focal region with a well-defined mass lesion eroding into the lumen as defined on the follow-up PET/CT suggests a potentially malignant lesion.

tumors, 20% were head and neck cancers, 11% were uroepithelial tumors and only 4.5% were colorectal cancers. The same study also identified 148 patients who developed lung cancer preceded by development of another primary cancer. Of these, 20% were head and neck cancers, 10% were uroepithelial cancers and 6% were colorectal cancers.

Conclusion

This study highlights the need to carefully evaluate PET/CT studies of lung and head and neck cancers for second malignancies. Improved lesion detectability and higher lesion contrast achieved with ToF PET and high-quality CT with contrast and thin slices should help delineation and characterization of such early second malignancies. ■

References:
[1] McCurdy et al. *Radiother Oncol*. July 2012; 104(1): 52-57.
[2] Edet Sanson et al. *Radiotherapy and Oncology*. 102 (2012): 251–257.
[3] Duchateau et al. *Chest*. 2005; 127: 1152–1158.

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing info can be found on pages 54-56.

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Examination Protocol

Scanner: Biograph mCT Flow

PET	
Injected dose	370 MBq (10 mCi) ^{18}F-FDG
Scan delay	1 hour
Acquisition	Continuous bed motion, uniform table speed (1.0 mm/sec)

CT	*Whole-body contrast*
Tube voltage	120 kV
Tube current	82 eff mAs
Slice collimation	64 x 0.6 mm
Slice thickness	5 mm

Case 8

Detection of Small Skull Metastases with ^{18}F-FDG* PET/CT Acquired with FlowMotion in a Patient with Lung Carcinoma

By Koji Murakami, MD

Data courtesy of Keio University Hospital, Tokyo, Japan

History
A 72-year-old man, who had a mass in the right lung that was detected on a chest radiograph and was subsequently proven to be squamous cell carcinoma on the histopathology, was referred for Fludeoxyglucose F 18 (^{18}F-FDG) PET/CT for initial staging. The study was performed 1 hour following a 6.6 mCi (244 MBq) IV injection of ^{18}F-FDG on a Biograph mCT Flow™**. Using FlowMotion™, data was acquired using continuous bed motion (CBM) instead of conventional step-and-shoot methods.

Following a low-dose non-contrast CT, CBM PET acquisition, using variable table speeds, was performed (*Figure 1*). This enabled an integrated acquisition of respiratory-gated PET in the thoracic region. A faster acquisition was used in the pelvis and upper thigh because of the lower clinical significance in the patient's specific situation.

FlowMotion acquisition allowed for the uniform axial noise level throughout the entire scan range. This resulted in well-maintained image quality at the edges of the axial field of view (FOV). With the conventional step-and-shoot method, the edges of the scan range usually show higher noise levels. Whole-body PET was reconstructed using ultraHD•PET (Time-of-Flight [ToF] and point spread function [PSF] reconstruction combined) at a 200x200 matrix. HD•Chest images were reconstructed separately using respiratory-gated PET data from the thorax reconstructed separately.

Diagnosis
The PET/CT images showed a hypermetabolic primary lung tumor in the upper right lobe (maximum diameter of 3.25 cm), with large mediastinal and right supraclavicular nodal metastases. The PET/CT also delineated a small solitary metastasis in the skull towards the midline. The presence of gross nodal metastases and a solitary skeletal metastasis in the skull reflected advanced disease. As such, chemoradiation was the only treatment option.

Comments
PET/CT defined the primary tumor and mediastinal and supraclavicular metastases. Since the lung and mediastinal lesions were quite large and ^{18}F-FDG- avid, there was no additional information obtained by respiratory-gated PET or HD•Chest images, both of which enable motion management for tumors moving with respiration. However, PET/CT showed a small slightly hypermetabolic bone metastasis exactly at the top of the skull. A small lesion in that area may be missed on conventional step-and-shoot

* Indications and important safety information on Fludeoxyglucose F 18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

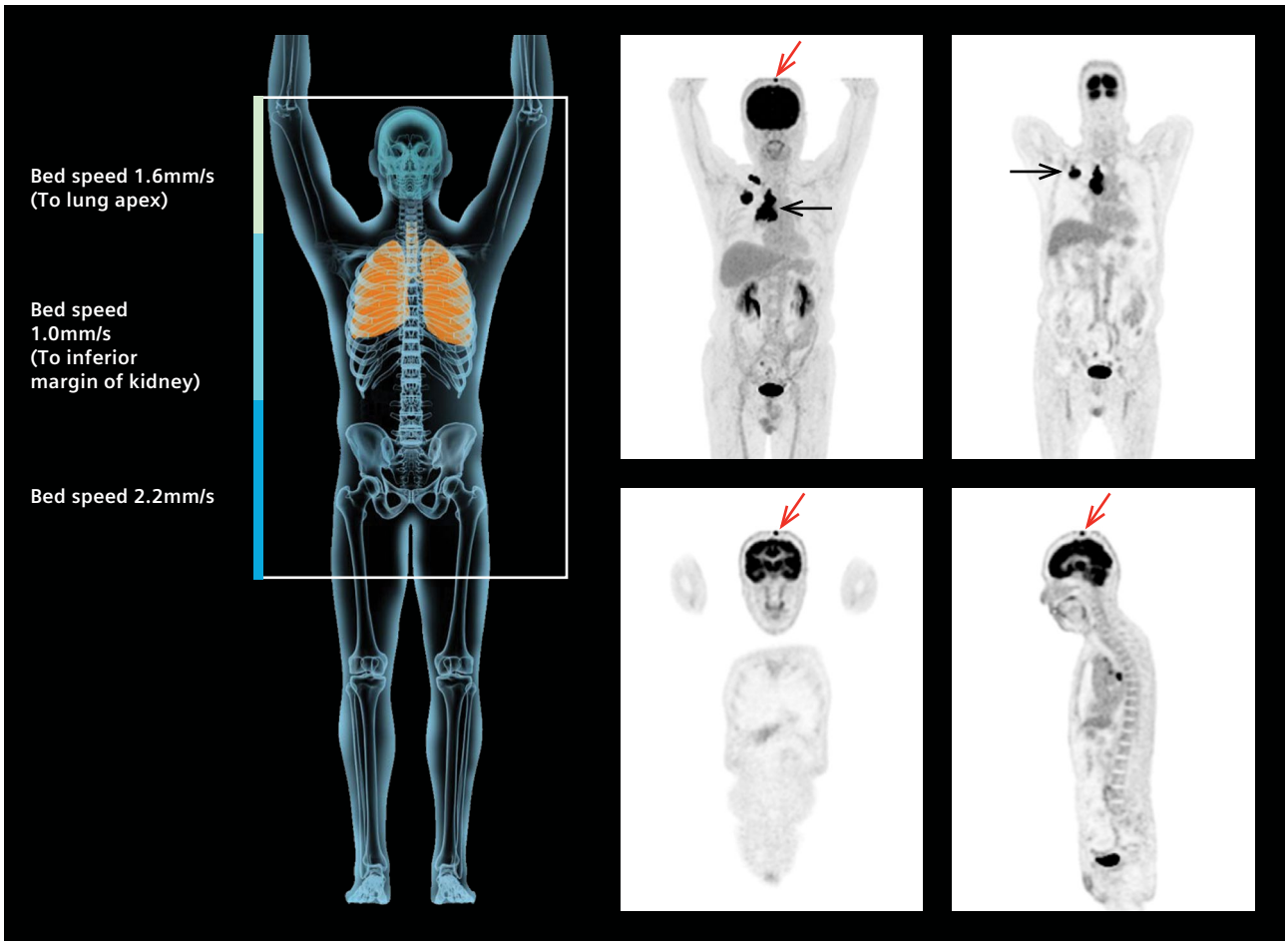

Figure 1: FlowMotion's variable table speed acquisition enables integrated respiratory gating of the thorax and upper abdomen. Whole-body PET maximum intensity projection (MIP) and multiplanar reconstruction (MPR) images show a large hypermetabolic lesion in the upper right lobe with large matted mediastinal nodal metastases and nodal metastases in the right supraclavicular region (*black arrows*). A small focal area of increased uptake is visible in the skull (*red arrow*), almost at the middle and just left of the midline. This also appears to be a solitary focal skeletal metastasis. No other skeletal lesion or distant metastasis is visible.

scanning since the noise level at the edge of the axial scan range is higher. With FlowMotion, though, the noise level throughout the entire scan range was uniform. This maintained image quality at the edges of the scan range, which is evident from the well-maintained image quality at the top of the skull seen in the PET images. FlowMotion enabled clear visualization of the small skull metastases that showed mildly increased ^{18}F-FDG uptake.

Although PET/CT showed the extent of the primary tumor and mediastinal and supraclavicular nodal metastases, the lesions were large enough to be determined by CT only. Based on the CT findings the patient would be staged at T2 N3, since tumor size is more than 3 cm and ipsilateral hilar, subcarinal and right supraclavicular nodal metastases are visible. But, PET/CT in this patient detected a small solitary focal skeletal metastasis in the skull, changing the stage to stage IV (T2, N3, M1). And although a small lytic area is visible on the CT corresponding to the ^{18}F-FDG-avid skull metastases, it would unlikely be identified on the evaluation of a routine CT-only scan. Due to the functional imaging provided by ^{18}F-FDG PET/CT, this small skeletal lesion was identified, and it led to a change in disease staging.

Conclusion

FlowMotion's CBM provides a uniform axial noise level throughout the entire scan range and, as a result, maintains image quality at the edges of scans. In this specific case, the maintained image quality at the edge of the scan helped to visualize a small lesion at the very top of the patient's skull. ■

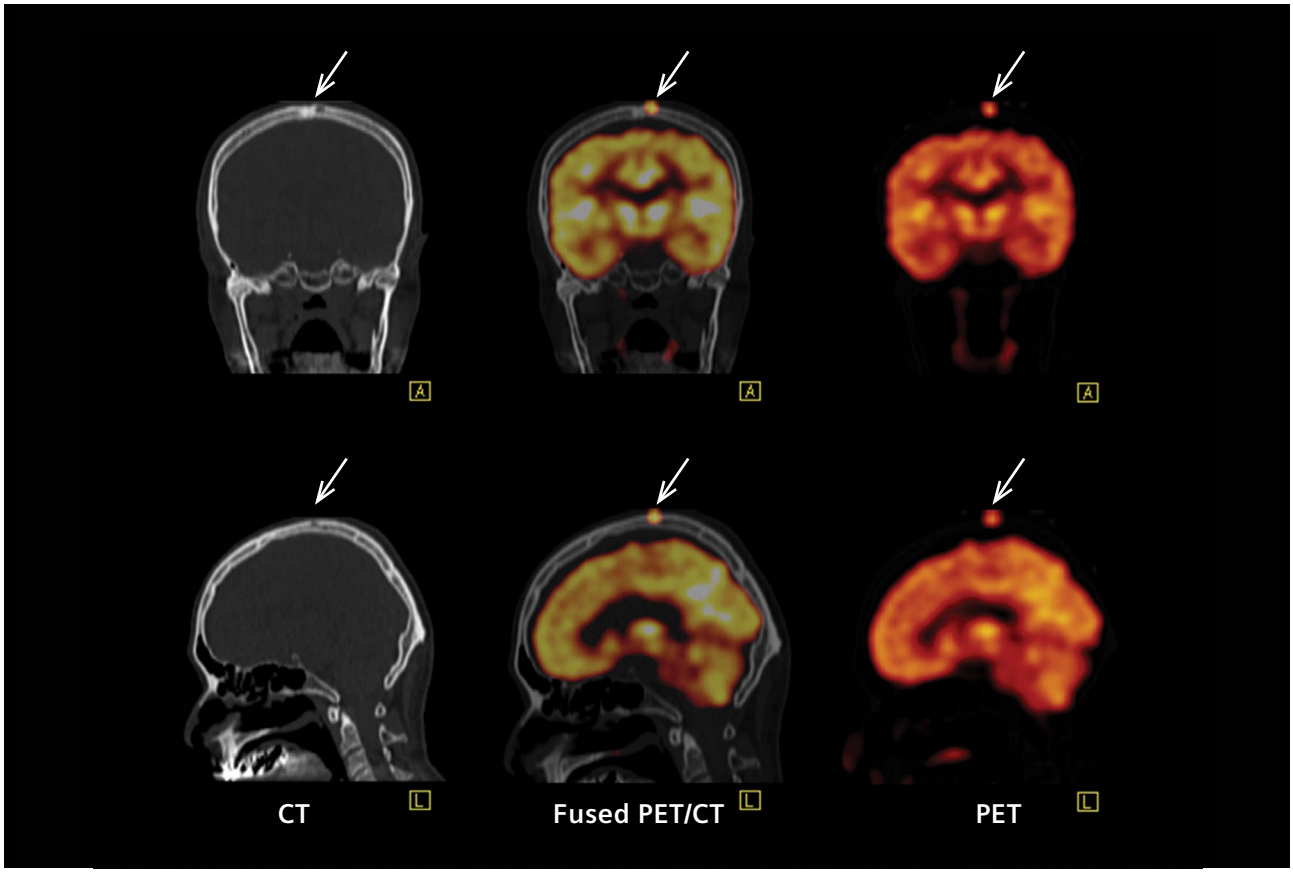

Figure 2: CT, PET and fused PET/CT of the head show a small focal hypermetabolic lesion in the middle of the skull, just left of the midline. CT shows a small lytic lesion involving the outer cortex of the left parietal bone, just to the left of the vertex that corresponds exactly to the focal hypermetabolic lesion on PET—thus suggesting a lytic metastasis.

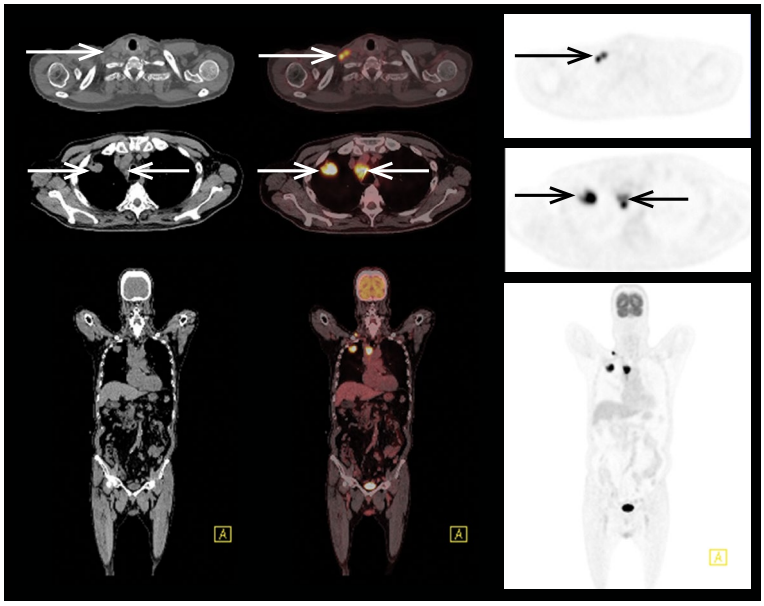

Figure 3: CT, PET and fused PET/CT images show ^{18}F-FDG-avid right upper lobar mass (*arrows*) and enlarged hypermetabolic right supraclavicular and mediastinal (right paratracheal) lymph nodal metastases *(arrows)*.

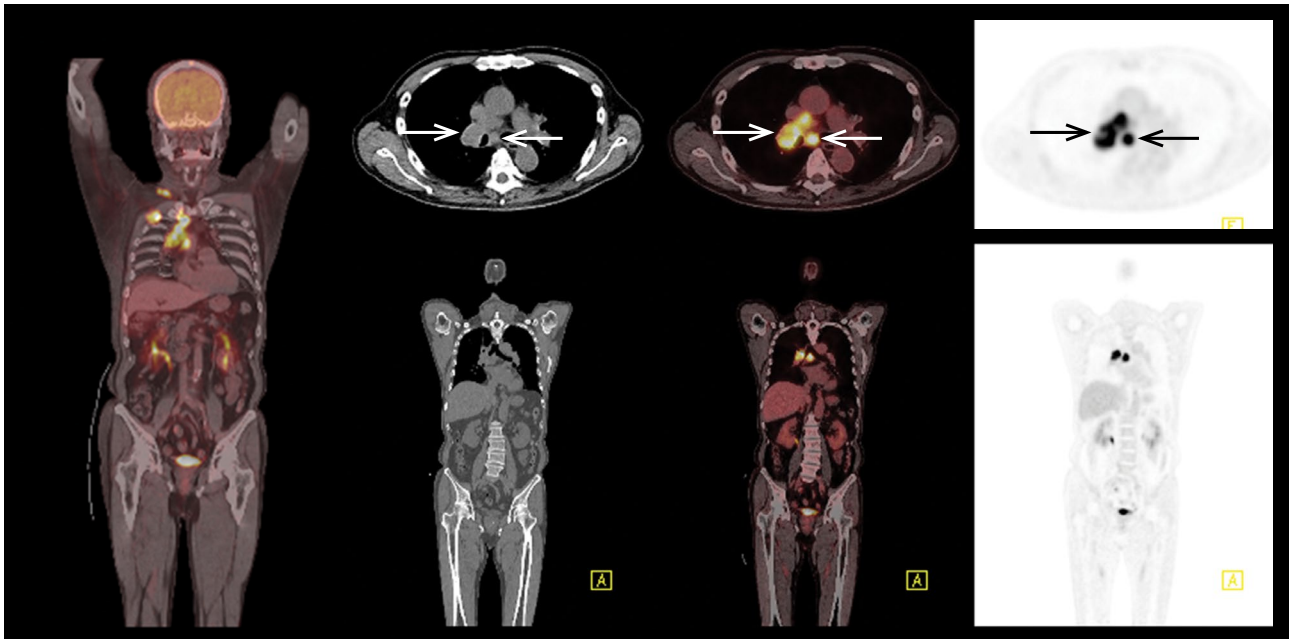

Figure 4: CT, PET and fused PET/CT images show matted enlarged hypermetabolic mediastinal nodal metastases involving the right hilar and subcarinal nodal groups.

Examination Protocol

Scanner: Biograph mCT Flow

PET	
Injected dose	6.6 mCi (244 MBq) ^{18}F-FDG
Scan delay	60 min
Scan speed	Zone 1, 1.6 mm/s; Zone 2, 1.0 mm/s; Zone 3, 2.2 mm/s
Acquisition	FlowMotion, continuous bed motion with variable speeds

CT	Low-dose non-contrast
Tube voltage	100 kV
Tube current	50 mAs
Slice collimation	3 mm
Slice thickness	5 mm

* Indications and Important safety information on Fludeoxyglucose F18 injection can be found on page 25. The full prescribing information can be found on pages 54-56.

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Tips & Tricks: Setting Scan Range on Biograph mCT Flow

Biograph mCT Flow™* supports two modes of bed motion, conventional stop-and-go (S&G) or the revolutionary FlowMotion™. With FlowMotion, the bed is moved continuously through the PET axial field of view (FOV). For PET/CT exams, both modes allow an alignment between the PET and CT data.

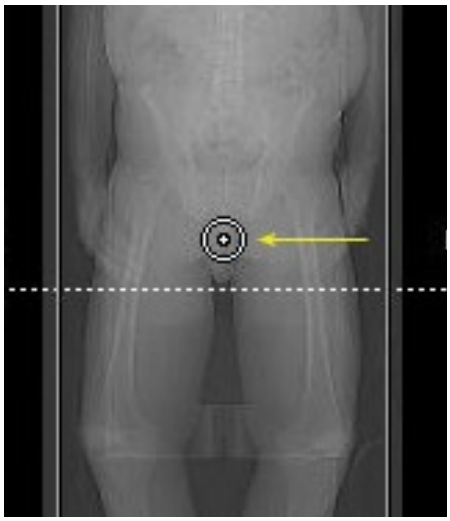


Figure 1: Small circle in the center to adjust axial range (*yellow arrow*).

Setting the Scan Range for FlowMotion
Setting the scan range for FlowMotion differs from stop-and-go. One change is that any start and stop position can be chosen by FlowMotion, whereas stop-and-go needs to start and stop at discrete bed positions. The second difference is that FlowMotion acquisition time is defined by the bed speed. Tables 1 and 2 convert the acquisition times between stop-and-go min/bed and FlowMotion bed speed. After acquiring the topogram, the scan range is indicated visually in the PET Planning window by a rectangular box.

> **Trick:** Double click in the PET planning window to view an enlarged topogram. Double click again to return to the standard view.

Define the Area to be Scanned in PET Planning Window
Adjust the position of the axial range by dragging the small white circle in the center of the scan range up or down with the left mouse (*Figure 1*).

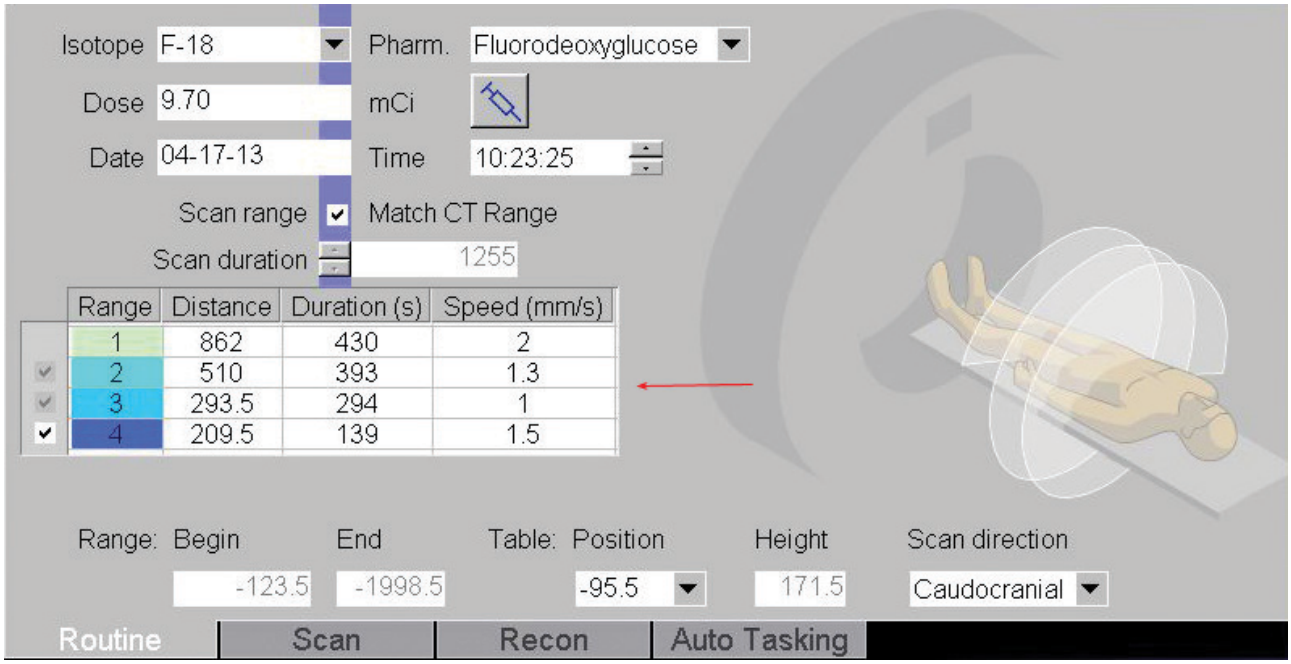


Figure 2: Up to four zones can be easily added with different distance, duration and speed.

Define up to Four PET Zones in Routine Task Card

In the routine task card, create from 1 to 4 zones with different bed speeds by checking the boxes to the left of the range column. Define the speed between 0.1 mm/s and 10.0 mm/s for each range in the speed column (*Figure 2*).

> **Trick:** Use Tables 1 and 2 to convert minutes per bed position to Biograph mCT Flow imaging protocols of mm per second. Note there are different values for a scanner with or without TrueV.

Redefine Scan Range in PET Planning Window

Scan range is typically defined by the protocol, but can be redefined by dragging the scan range reference lines in the PET Planning window (*Figure 3*). Changing the length of a range in the PET planning window changes the distance value on the routine task card (*Figure 2*).

Biograph mCT Flow		Biograph mCT Flow with TrueV	
S&G Acquisition Time (*min/bed*)	**FlowMotion Speed (*mm/s*)**	**S&G Acquisition Time (*min/bed*)**	**FlowMotion Speed (*mm/s*)**
1:00	1.5	1:00	2.1
1:48	0.8	1:48	1.2
2:00	0.7	2:00	1.1
2:30	0.6	2:48	0.8
3:00	0.5	3:00	0.7
4:00	0.4	4:00	0.5
5:00	0.3	5:00	0.4
6:00	0.2	8:00	0.3
10:00	0.1	10:00	0.2

Table 1: Stop-and-go acquisition times mapped to FlowMotion bed speed to achieve equivalent image quality on Biograph mCT Flow.

Table 2: Stop-and-go acquisition times mapped to FlowMotion bed speed to achieve equivalent image quality on Biograph mCT Flow with TrueV.

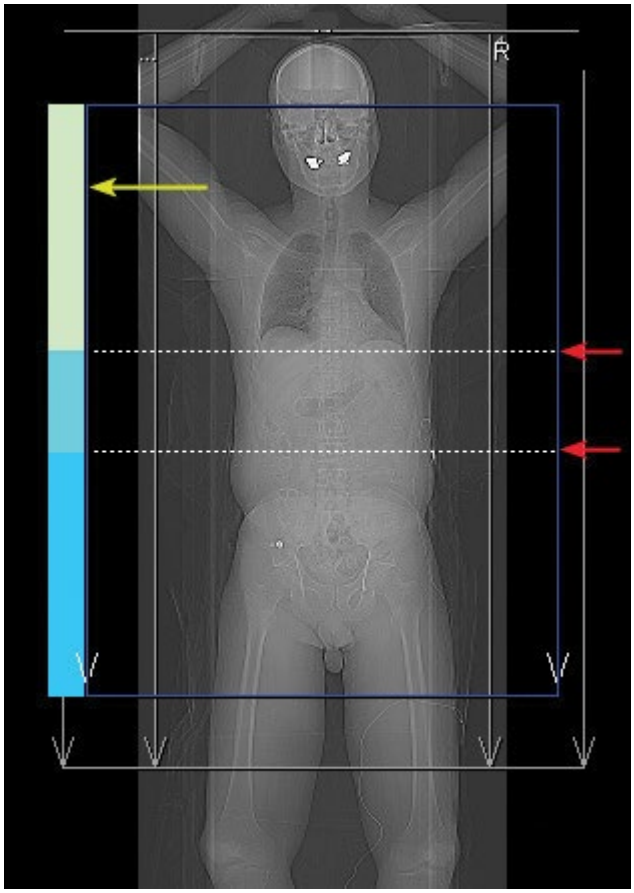


Figure 3: Scan range reference bar (*yellow arrow*). Scan range reference lines (*red arrows*).

Tip: Scan ranges are indicated visually by color coded bars on the scan reference bar on the left side of the PET Planning window (*Figure 3*) corresponding to the colored zone numbers in the range column of the routine task card (*Figure 2*).

Trick: The length of ranges can also be changed easily by dragging the dotted lines in the PET Planning window. Changing the length of a range in the PET Planning window changes the distance value on the routine task card.

Trick: For FlowMotion protocols, on the routine task card, if you check Scan Range - Match CT Range (*Figure 4*), *syngo*® automatically adjusts the CT field of view to match the PET field of view. Correspondingly, if the CT range is changed, the PET range is automatically changed to match. If Match CT Range is left unchecked, the CT and PET ranges will not automatically match (*Table 3*). ■

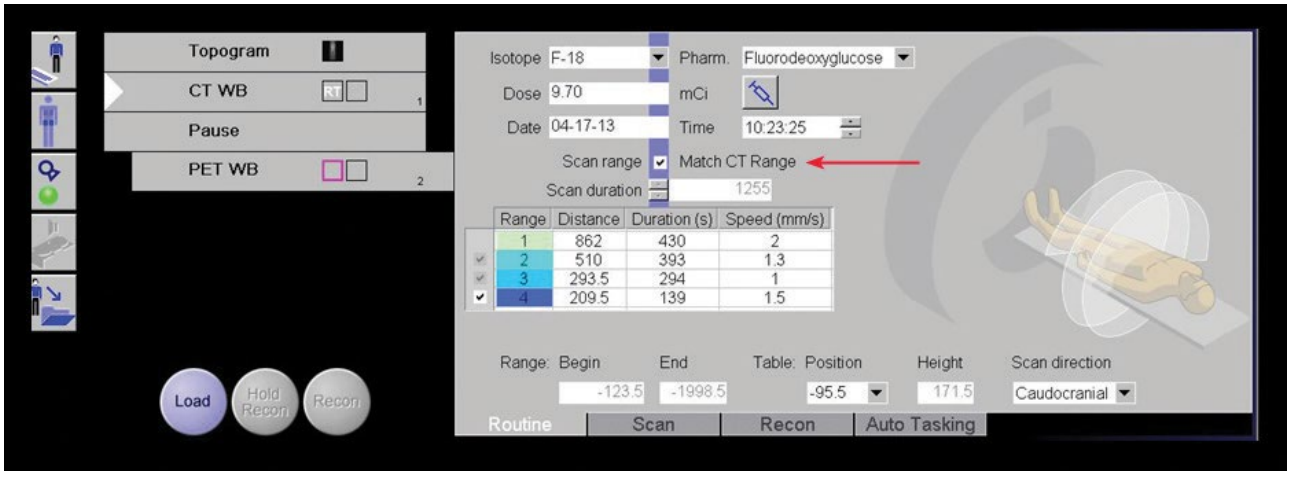


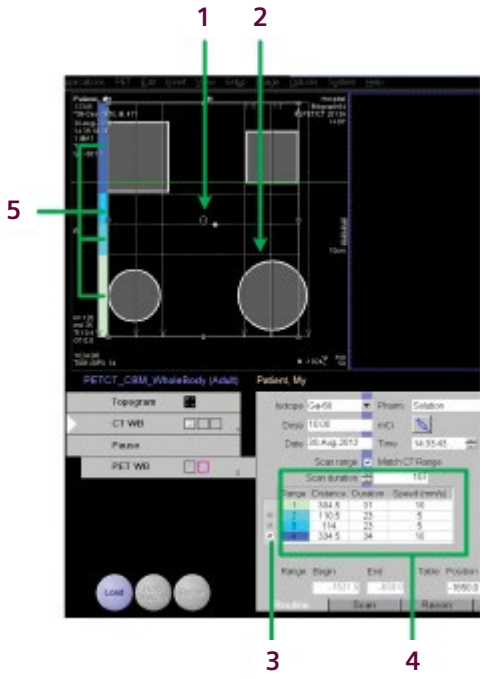
Figure 4: Scan Range - Match CT Range.

Match CT Range	Match CT Slice Location	Behavior of PET/CT Planning
Checked	Checked	CT range snaps automatically to PET scan range. The PET image slice location and thickness is then matched to the CT.
Unchecked	Checked	The CT and PET scan ranges are independently defined. The PET image slice location and thickness will be matched to the CT for the planned PET scan range.

Table 3: Match CT Range option to behavior of PET/CT planning.

Overview: Setting Scan Range in FlowMotion Planning Window

1. Adjust the position of the axial range by dragging the small white circle
2. Drag the scan range reference lines to further define scan range
3. Click the box to add a new zone
4. Define the speed for each zone
5. Color-coded PET FlowMotion regions correspond to the color coded zones on the routine subtask card



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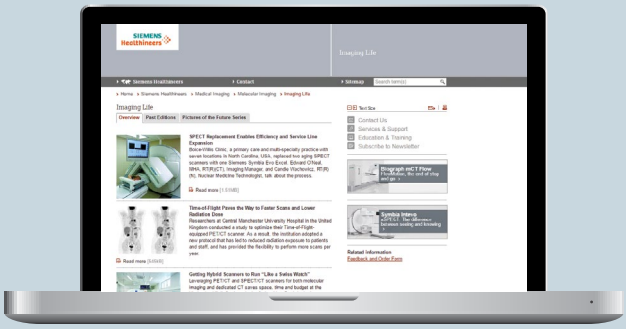

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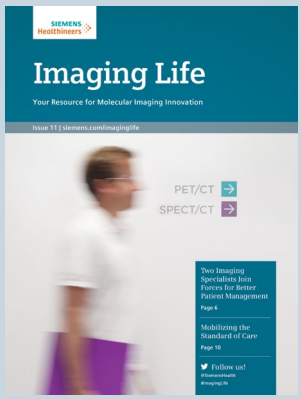

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Fludeoxyglucose F 18 Injection safely and effectively. See full prescribing information for Fludeoxyglucose F 18 Injection.

Fludeoxyglucose F 18 Injection, USP
For intravenous use
Initial U.S. Approval: 2005

RECENT MAJOR CHANGES

Warnings and Precautions (5.1, 5.2)	7/2010
Adverse Reactions (6)	7/2010

INDICATIONS AND USAGE

Fludeoxyglucose F18 Injection is indicated for positron emission tomography (PET) imaging in the following settings:

- Oncology: For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.
- Cardiology: For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.
- Neurology: For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures (1).

DOSAGE AND ADMINISTRATION

Fludeoxyglucose F 18 Injection emits radiation. Use procedures to minimize radiation exposure. Screen for blood glucose abnormalities.

- In the oncology and neurology settings, instruct patients to fast for 4 to 6 hours prior to the drug's injection. Consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to the drug's administration (5.2).
- In the cardiology setting, administration of glucose-containing food or liquids (e.g., 50 to 75 grams) prior to the drug's injection facilitates localization of cardiac ischemia (2.3).

Aseptically withdraw Fludeoxyglucose F 18 Injection from its container and administer by intravenous injection (2).

The recommended dose:

- for adults is 5 to 10 mCi (185 to 370 MBq), in all indicated clinical settings (2.1).
- for pediatric patients is 2.6 mCi in the neurology setting (2.2).

Initiate imaging within 40 minutes following drug injection; acquire static emission images 30 to 100 minutes from time of injection (2).

DOSAGE FORMS AND STRENGTHS

Multi-dose 30mL and 50mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) Fludeoxyglucose F 18 Injection and 4.5mg of sodium chloride with 0.1 to 0.5% w/w ethanol as a stabilizer (approximately 15 to 50 mL volume) for intravenous administration (3).

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

- Radiation risks: use smallest dose necessary for imaging (5.1).
- Blood glucose abnormalities: may cause suboptimal imaging (5.2).

ADVERSE REACTIONS

Hypersensitivity reactions have occurred; have emergency resuscitation equipment and personnel immediately available (6).

To report SUSPECTED ADVERSE REACTIONS, contact PETNET Solutions, Inc. at 877-473-8638 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy Category C: No human or animal data. Consider alternative diagnostics; use only if clearly needed (8.1).

- Nursing mothers: Use alternatives to breast feeding (e.g., stored breast milk or infant formula) for at least 10 half-lives of radioactive decay, if Fludeoxyglucose F 18 Injection is administered to a woman who is breast-feeding (8.3).
- Pediatric Use: Safety and effectiveness in pediatric patients have not been established in the oncology and cardiology settings (8.4).

See 17 for PATIENT COUNSELING INFORMATION

Revised: 1/2016

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Fludeoxyglucose F 18 Injection is indicated for positron emission tomography (PET) imaging in the following settings:

1.1 Oncology

For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.

1.2 Cardiology

For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.

1.3 Neurology

For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

2 DOSAGE AND ADMINISTRATION

Fludeoxyglucose F 18 Injection emits radiation. Use procedures to minimize radiation exposure. Calculate the final dose from the end of synthesis (EOS) time using proper radioactive decay factors. Assay the final dose in a properly calibrated dose calibrator before administration to the patient [see Description (11.2)].

2.1 Recommended Dose for Adults

Within the oncology, cardiology and neurology settings, the recommended dose for adults is 5 to 10 mCi (185 to 370 MBq) as an intravenous injection.

2.2 Recommended Dose for Pediatric Patients

Within the neurology setting, the recommended dose for pediatric patients is 2.6 mCi, as an intravenous injection. The optimal dose adjustment on the basis of body size or weight has not been determined [see *Use in Special Populations (8.4)*].

2.3 Patient Preparation

- To minimize the radiation absorbed dose to the bladder, encourage adequate hydration. Encourage the patient to drink water or other fluids (as tolerated) in the 4 hours before their PET study.
- Encourage the patient to void as soon as the imaging study is completed and as often as possible thereafter for at least one hour.
- Screen patients for clinically significant blood glucose abnormalities by obtaining a history and/or laboratory tests [see *Warnings and Precautions (5.2)*]. Prior to Fludeoxyglucose F 18 PET imaging in the oncology and neurology settings, instruct patient to fast for 4 to 6 hours prior to the drug's injection.
- In the cardiology setting, administration of glucose-containing food or liquids (e.g., 50 to 75 grams) prior to Fludeoxyglucose F18 Injection facilitates localization of cardiac ischemia

2.4 Radiation Dosimetry

The estimated human absorbed radiation doses (rem/mCi) to a newborn (3.4 kg), 1-year old (9.8 kg), 5-year old (19 kg), 10-year old (32 kg), 15-year old (57 kg), and adult (70 kg) from intravenous administration of Fludeoxyglucose F 18 Injection are shown in Table 1. These estimates were calculated based on human[2] data and using the data published by the International Commission on Radiological Protection[4] for Fludeoxyglucose ^{18}F. The dosimetry data show that there are slight variations in absorbed radiation dose for various organs in each of the age groups. These dissimilarities in absorbed radiation dose are due to developmental age variations (e.g., organ size, location, and overall metabolic rate for each age group). The identified critical organs (in descending order) across all age groups evaluated are the urinary bladder, heart, pancreas, spleen, and lungs.

Table 1. Estimated Absorbed Radiation Doses (rem/mCi) After Intravenous Administration of Fludeoxyglucose F-18 Injection[a]

Organ	Newborn (3.4 kg)	1-year old (9.8 kg)	5-year old (19 kg)	10-year old (32 kg)	15-year old (57 kg)	Adult (70 kg)
Bladder wall[b]	4.3	1.7	0.93	0.60	0.40	0.32
Heart wall	2.4	1.2	0.70	0.44	0.29	0.22
Pancreas	2.2	0.68	0.33	0.25	0.13	0.096
Spleen	2.2	0.84	0.46	0.29	0.19	0.14
Lungs	0.96	0.38	0.20	0.13	0.092	0.064
Kidneys	0.81	0.34	0.19	0.13	0.089	0.074
Ovaries	0.80	0.8	0.19	0.11	0.058	0.053
Uterus	0.79	0.35	0.19	0.12	0.076	0.062
LLI wall *	0.69	0.28	0.15	0.097	0.060	0.051
Liver	0.69	0.31	0.17	0.11	0.076	0.058
Gallbladder wall	0.69	0.26	0.14	0.093	0.059	0.049
Small intestine	0.68	0.29	0.15	0.096	0.060	0.047
ULI wall **	0.67	0.27	0.15	0.090	0.057	0.046
Stomach wall	0.65	0.27	0.14	0.089	0.057	0.047
Adrenals	0.65	0.28	0.15	0.095	0.061	0.048
Testes	0.64	0.27	0.14	0.085	0.052	0.041
Red marrow	0.62	0.26	0.14	0.089	0.057	0.047
Thymus	0.61	0.26	0.14	0.086	0.056	0.044
Thyroid	0.61	0.26	0.13	0.080	0.049	0.039
Muscle	0.58	0.25	0.13	0.078	0.049	0.039
Bone surface	0.57	0.24	0.12	0.079	0.052	0.041
Breast	0.54	0.22	0.11	0.068	0.043	0.034
Skin	0.49	0.20	0.10	0.060	0.037	0.030
Brain	0.29	0.13	0.09	0.078	0.072	0.070
Other tissues	0.59	0.25	0.13	0.083	0.052	0.042

[a] MIRDOSE 2 software was used to calculate the radiation absorbed dose. Assumptions on the biodistribution based on data from Gallagher et al.[1] and Jones et al.[2]

[b] The dynamic bladder model with a uniform voiding frequency of 1.5 hours was used. *LLI = lower large intestine; **ULI = upper large intestine

2.5 Radiation Safety – Drug Handling

- Use waterproof gloves, effective radiation shielding, and appropriate safety measures when handling Fludeoxyglucose F 18 Injection to avoid unnecessary radiation exposure to the patient, occupational workers, clinical personnel and other persons.
- Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.
- Calculate the final dose from the end of synthesis (EOS) time using proper radioactive decay factors. Assay the final dose in a properly calibrated dose calibrator before administration to the patient [see *Description (11.2)*].
- The dose of Fludeoxyglucose F 18 used in a given patient should be minimized consistent with the objectives of the procedure, and the nature of the radiation detection devices employed.

2.6 Drug Preparation and Administration

- Calculate the necessary volume to administer based on calibration time and dose.
- Aseptically withdraw Fludeoxyglucose F 18 Injection from its container.
- Inspect Fludeoxyglucose F 18 Injection visually for particulate matter and discoloration before administration, whenever solution and container permit.
- Do not administer the drug if it contains particulate matter or discoloration; dispose of these unacceptable or unused preparations in a safe manner, in compliance with applicable regulations.
- Use Fludeoxyglucose F 18 Injection within 12 hours from the EOS.

2.7 Imaging Guidelines

- Initiate imaging within 40 minutes following Fludeoxyglucose F 18 Injection administration.
- Acquire static emission images 30 to 100 minutes from the time of injection.

3 DOSAGE FORMS AND STRENGTHS

Multiple-dose 30 mL and 50 mL glass vial containing 0.74 to 7.40 GBq/mL (20 to 200 mCi/mL) of Fludeoxyglucose F 18 Injection and 4.5 mg of sodium chloride with 0.1 to 0.5% w/w ethanol as a stabilizer (approximately 15 to 50 mL volume) for intravenous administration.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Radiation Risks

Radiation-emitting products, including Fludeoxyglucose F 18 Injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker [see *Dosage and Administration (2.5)*].

5.2 Blood Glucose Abnormalities

In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to Fludeoxyglucose F 18 Injection administration.

6 ADVERSE REACTIONS

Hypersensitivity reactions with pruritus, edema and rash have been reported in the post-marketing setting. Have emergency resuscitation equipment and personnel immediately available.

7 DRUG INTERACTIONS

The possibility of interactions of Fludeoxyglucose F 18 Injection with other drugs taken by patients undergoing PET imaging has not been studied.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with Fludeoxyglucose F 18 Injection. It is also not known whether Fludeoxyglucose F 18 Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Consider alternative diagnostic tests in a pregnant woman; administer Fludeoxyglucose F 18 Injection only if clearly needed.

8.3 Nursing Mothers

It is not known whether Fludeoxyglucose F 18 Injection is excreted in human milk. Consider alternative diagnostic tests in women who are breast-feeding. Use alternatives to breast feeding (e.g., stored breast milk or infant formula) for at least 10 half-lives of radioactive decay, if Fludeoxyglucose F 18 Injection is administered to a woman who is breast-feeding.

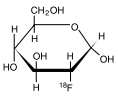
8.4 Pediatric Use

The safety and effectiveness of Fludeoxyglucose F 18 Injection in pediatric patients with epilepsy is established on the basis of studies in adult and pediatric patients. In pediatric patients with epilepsy, the recommended dose is 2.6 mCi. The optimal dose adjustment on the basis of body size or weight has not been determined. In the oncology or cardiology settings, the safety and effectiveness of Fludeoxyglucose F 18 Injection have not been established in pediatric patients.

11 DESCRIPTION

11.1 Chemical Characteristics

Fludeoxyglucose F 18 Injection is a positron emitting radiopharmaceutical that is used for diagnostic purposes in conjunction with positron emission tomography (PET) imaging. The active ingredient 2-deoxy-2-[^{18}F]fluoro-D-glucose has the molecular formula of $C_6H_{11}{}^{18}FO_5$ with a molecular weight of 181.26, and has the following chemical structure:



Fludeoxyglucose F 18 Injection is provided as a ready to use sterile, pyrogen free, clear, colorless solution. Each mL contains between 0.740 to 7.40GBq (20.0 to 200 mCi) of 2-deoxy-2-[^{18}F]fluoro-D-glucose at the EOS, 4.5 mg of sodium chloride and 0.1 to 0.5% w/w ethanol as a stabilizer. The pH of the solution is between 4.5 and 7.5. The solution is packaged in a multiple-dose glass vial and does not contain any preservative.

11.2 Physical Characteristics

Fluorine F 18 decays by emitting positron to Oxygen O 16 (stable) and has a physical half-life of 109.7 minutes. The principal photons useful for imaging are the dual 511 keV gamma photons, that are produced and emitted simultaneously in opposite direction when the positron interacts with an electron (Table 2).

Table 2. Pricipal Radiation Emission Data for Fluorine F18

Radiation/Emission	% Per Disintegration	Mean Energy
Positron (b+)	96.73	249.8 keV
Gamma (±)*	193.46	511.0 keV

*Produced by positron annihilation

From: Kocher, D.C. Radioactive Decay Tables DOE/TIC-I 1026, 89 (1981)

The specific gamma ray constant (point source air kerma coefficient) for fluorine F 18 is 5.7 R/hr/mCi (1.35 x 10^{-6} Gy/hr/kBq) at 1 cm. The half-value layer (HVL) for the 511 keV photons is 4 mm lead (Pb). The range of attenuation coefficients for this radionuclide as a function of lead shield thickness is shown in Table 3. For example, the interposition of an 8 mm thickness of Pb, with a coefficient of attenuation of 0.25, will decrease the external radiation by 75%.

Table 3. Radiation Attenuation of 511 keV Photons by lead (Pb) shielding

Shield thickness (Pb) mm	Coefficient of attenuation
0	0.00
4	0.50
8	0.25
13	0.10
26	0.01
39	0.001
52	0.0001

For use in correcting for physical decay of this radionuclide, the fractions remaining at selected intervals after calibration are shown in Table 4.

Table 4. Physical Decay Chart for Fluorine F18

Minutes	Fraction Remaining
0*	1.000
15	0.909
30	0.826
60	0.683
110	0.500
220	0.250

*calibration time

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Fludeoxyglucose F 18 is a glucose analog that concentrates in cells that rely upon glucose as an energy source, or in cells whose dependence on glucose increases under pathophysiological conditions. Fludeoxyglucose F 18 is transported through the cell membrane by facilitative glucose transporter proteins and is phosphorylated within the cell to [^{18}F] FDG-6-phosphate by the enzyme hexokinase. Once phosphorylated it cannot exit until it is dephosphorylated by glucose-6-phosphatase. Therefore, within a given tissue or pathophysiological process, the retention and clearance of Fludeoxyglucose F 18 reflect a balance involving glucose transporter, hexokinase and glucose-6-phosphatase activities. When allowance is made for the kinetic differences between glucose and Fludeoxyglucose F 18 transport and phosphorylation (expressed as the ‚lumped constant" ratio), Fludeoxyglucose F 18 is used to assess glucose metabolism.

In comparison to background activity of the specific organ or tissue type, regions of decreased or absent uptake of Fludeoxyglucose F 18 reflect the decrease or absence of glucose metabolism. Regions of increased uptake of Fludeoxyglucose F 18 reflect greater than normal rates of glucose metabolism.

12.2 Pharmacodynamics

Fludeoxyglucose F 18 Injection is rapidly distributed to all organs of the body after intravenous administration. After background clearance of Fludeoxyglucose F 18 Injection, optimal PET imaging is generally achieved between 30 to 40 minutes after administration.

In cancer, the cells are generally characterized by enhanced glucose metabolism partially due to (1) an increase in activity of glucose transporters, (2) an increased rate of phosphorylation activity, (3) a reduction of phosphatase activity or, (4) a dynamic alteration in the balance among all these processes. However, glucose metabolism of cancer as reflected by Fludeoxyglucose F 18 accumulation shows considerable variability. Depending on tumor type, stage, and location, Fludeoxyglucose F 18 accumulation may be increased, normal, or decreased. Also, inflammatory cells can have the same variability of uptake of Fludeoxyglucose F 18.

In the heart, under normal aerobic conditions, the myocardium meets the bulk of its energy requirements by oxidizing free fatty acids. Most of the exogenous glucose taken up by the myocyte is converted into glycogen. However, under ischemic conditions, the oxidation of free fatty acids decreases, exogenous glucose becomes the preferred myocardial sub strate, glycolysis is stimulated, and glucose taken up by the myocyte is metabolized immediately instead of being converted into glycogen. Under these condi-

tions, phosphorylated Fludeoxyglucose F 18 accumulates in the myocyte and can be detected with PET imaging.

In the brain, cells normally rely on aerobic metabolism. In epilepsy, the glucose metabolism varies. Generally, during a seizure, glucose metabolism increases. Interictally, the seizure focus tends to be hypometabolic.

12.3 Pharmacokinetics

Distribution: In four healthy male volunteers, receiving an intravenous administration of 30 seconds induration, the arterial blood level profile for Fludeoxyglucose F 18 decayed triexponentially. The effective half-life ranges of the three phases were 0.2 to 0.3 minutes, 10 to 13 minutes with a mean and standard deviation (STD) of 11.6 (±) 1.1 min, and 80 to 95 minutes with a mean and STD of 88 (±) 4 min.

Plasma protein binding of Fludeoxyglucose F 18 has not been studied.

Metabolism: Fludeoxyglucose F 18 is transported into cells and phosphorylated to [^{18}F]-FDG-6- phosphate at a rate proportional to the rate of glucose utilization within that tissue. [F18]-FDG-6-phosphate presumably is metabolized to 2-deoxy-2-[F18]fluoro-6-phospho-D-mannose([F 18]FDM-6-phosphate).

Fludeoxyglucose F 18 Injection may contain several impurities (e.g., 2-deoxy-2-chloro-D-glucose (ClDG)). Biodistribution and metabolism of ClDG are presumed to be similar to Fludeoxyglucose F 18 and would be expected to result in intracellular formation of 2-deoxy-2-chloro-6-phospho-D-glucose (ClDG-6-phosphate) and 2-deoxy-2-chloro-6-phospho-D-mannose (ClDM-6-phosphate). The phosphorylated deoxyglucose compounds are dephosphorylated and the resulting compounds (FDG, FDM, ClDG, and ClDM) presumably leave cells by passive diffusion. Fludeoxyglucose F 18 and related compounds are cleared from non-cardiac tissues within 3 to 24 hours after administration. Clearance from the cardiac tissue may require more than 96 hours. Fludeoxyglucose F 18 that is not involved in glucose metabolism in any tissue is then excreted in the urine.

Elimination: Fludeoxyglucose F 18 is cleared from most tissues within 24 hours and can be eliminated from the body unchanged in the urine. Three elimination phases have been identified in the reviewed literature. Within 33 minutes, a mean of 3.9% of the administrated radioactive dose was measured in the urine. The amount of radiation exposure of the urinary bladder at two hours post-administration suggests that 20.6% (mean) of the radioactive dose was present in the bladder.

Special Populations:

The pharmacokinetics of Fludeoxyglucose F 18 Injection have not been studied in renally-impaired, hepatically impaired or pediatric patients. Fludeoxyglucose F 18 is eliminated through the renal system. Avoid excessive radiation exposure to this organ system and adjacent tissues.

The effects of fasting, varying blood sugar levels, conditions of glucose intolerance, and diabetes mellitus on Fludeoxyglucose F 18 distribution in humans have not been ascertained [*see Warnings and Precautions (5.2)*].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been performed to evaluate the Fludeoxyglucose F 18 Injection carcinogenic potential, mutagenic potential or effects on fertility.

14 CLINICAL STUDIES

14.1 Oncology

The efficacy of Fludeoxyglucose F 18 Injection in positron emission tomography cancer imaging was demonstrated in 16 independent studies. These studies prospectively evaluated the use of Fludeoxyglucose F 18 in patients with suspected or known malignancies, including non-small cell lung cancer, colo-rectal, pancreatic, breast, thyroid, melanoma, Hodgkin's and non-Hodgkin's lymphoma, and various types of metastatic cancers to lung, liver, bone, and axillary nodes. All these studies had at least 50 patients and used pathology as a standard of truth. The Fludeoxyglucose F 18 Injection doses in the studies ranged from 200 MBq to 740 MBq with a median and mean dose of 370 MBq.

In the studies, the diagnostic performance of Fludeoxyglucose F 18 Injection varied with the type of cancer, size of cancer, and other clinical conditions. False negative and false positive scans were observed. Negative Fludeoxyglucose F 18 Injection PET scans do not exclude the diagnosis of cancer. Positive Fludeoxyglucose F 18 Injection PET scans can not replace pathology to establish a diagnosis of cancer. Non-malignant conditions such as fungal infections, inflammatory processes and benign tumors have patterns of increased glucose metabolism that may give rise to false-positive scans. The efficacy of Fludeoxyglucose F 18 Injection PET imaging in cancer screening was not studied.

14.2 Cardiology

The efficacy of Fludeoxyglucose F 18 Injection for cardiac use was demonstrated in ten independent, prospective studies of patients with coronary artery disease and chronic left ventricular systolic dysfunction who were scheduled to undergo coronary revascularization. Before revascularization, patients underwent PET imaging with Fludeoxyglucose F 18 Injection (74 to 370 MBq, 2 to 10 mCi) and perfusion imaging with other diagnostic radiopharmaceuticals. Doses of Fludeoxyglucose F 18 Injection ranged from 74 to 370 MBq (2 to 10 mCi). Segmental, left ventricular, wall-motion assessments of asynergic areas made before revascularization were compared in a blinded manner to assessments made after successful revascularization to identify myocardial segments with functional recovery.

Left ventricular myocardial segments were predicted to have reversible loss of systolic function if they showed Fludeoxyglucose F 18 accumulation and reduced perfusion (i.e., flow-metabolism mismatch). Conversely, myocardial segments were predicted to have irreversible loss of systolic function if they showed reductions in both Fludeoxyglucose F 18 accumulation and perfusion (i.e., matched defects).

Findings of flow-metabolism mismatch in a myocardial segment may suggest that successful revascularization will restore myocardial function in that segment. However, false-positive tests occur regularly, and the decision to have a patient undergo revascularization should not be based on PET findings alone. Similarly, findings of a matched defect in a myocardial segment may suggest that myocardial function will not recover in that segment, even if it is successfully revascularized. However, false-negative tests occur regularly, and the decision to recommend against coronary revascularization, or to recommend a cardiac transplant, should not be based on PET findings alone. The reversibility of segmental dysfunction as predicted with Fludeoxyglucose F 18 PET imaging depends on successful coronary revascularization. Therefore, in patients with a low likelihood of successful revascularization, the diagnostic usefulness of PET imaging with Fludeoxyglucose F 18 Injection is more limited.

14.3 Neurology

In a prospective, open label trial, Fludeoxyglucose F 18 Injection was evaluated in 86 patients with epilepsy. Each patient received a dose of Fludeoxyglucose F 18 Injection in the range of 185 to 370 MBq (5 to 10 mCi). The mean age was 16.4 years (range: 4 months to 58 years; of these, 42 patients were less than 12 years and 16 patients were less than 2 years old). Patients had a known diagnosis of complex partial epilepsy and were under evaluation for surgical treatment of their seizure disorder. Seizure foci had been previously identified on ictal EEGs and sphenoidal EEGs. Fludeoxyglucose F 18 Injection PET imaging confirmed previous diagnostic findings in 16% (14/87) of the patients; in 34% (30/87) of the patients, Fludeoxyglucose F 18 Injection PET images provided new findings. In 32% (27/87), imaging with Fludeoxyglucose F 18 Injection was inconclusive. The impact of these imaging findings on clinical outcomes is not known.

Several other studies comparing imaging with Fludeoxyglucose F 18 Injection results to subsphenoidal EEG, MRI and/or surgical findings supported the concept that the degree of hypometabolism corresponds to areas of confirmed epileptogenic foci. The safety and effectiveness of Fludeoxyglucose F 18 Injection to distinguish idiopathic epileptogenic foci from tumors or other brain lesions that may cause seizures have not been established.

15 REFERENCES

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2. Jones S.C., Alavi, A., Christman D., Montanez, I., Wolf, A.P., and Reivich M. "The radiation dosimetry of 2 [F-18] fluoro-2-deoxy-D-glucose in man," J Nucl Med, 1982; 23, 613-617.
3. Kocher, D.C. "Radioactive Decay Tables: A handbook of decay data for application to radiation dosimetry and radiological assessments," 1981, DOE/TIC-I 1026, 89.
4. ICRP Publication 53, Volume 18, No. I-4,1987, pages 75-76.

16 HOW SUPPLIED/STORAGE AND DRUG HANDLING

Fludeoxyglucose F 18 Injection is supplied in a multi-dose, capped 30 mL and 50 mL glass vial containing between 0.740 to 7.40GBq/mL (20 to 200 mCi/mL), of no carrier added 2deoxy-2-[F 18] fluoro-D-glucose, at end of synthesis, in approximately 15 to 50 mL. The contents of each vial are sterile, pyrogen-free and preservative-free.

NDC 40028-511-30; 40028-511-50

Receipt, transfer, handling, possession, or use of this product is subject to the radioactive material regulations and licensing requirements of the U.S. Nuclear Regulatory Commission, Agreement States or Licensing States as appropriate.

Store the Fludeoxyglucose F 18 Injection vial upright in a lead shielded container at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Store and dispose of Fludeoxyglucose F 18 Injection in accordance with the regulations and a general license, or its equivalent, of an Agreement State or a Licensing State.

The expiration date and time are provided on the container label. Use Fludeoxyglucose F 18 Injection within 12 hours from the EOS time.

17 PATIENT COUNSELING INFORMATION

Instruct patients in procedures that increase renal clearance of radioactivity. Encourage patients to:

- drink water or other fluids (as tolerated) in the 4 hours before their PET study.
- void as soon as the imaging study is completed and as often as possible thereafter for at least one hour.

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