
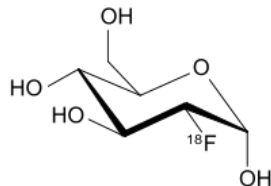


# [<sup>18</sup>F]fluorodeoxyglucose, <sup>18</sup>F-FDG or FDG

## 2-deoxy-2-[<sup>18</sup>F]-fluoro-D-glucose

<b>Radiopharmaceutical Name</b>	2-deoxy-2-[ <sup>18</sup> F]-fluoro-D-glucose Abbreviations: [ <sup>18</sup> F]fluorodeoxyglucose, <sup>18</sup> F-FDG or FDG	
<b>Radiopharmaceutical Image</b>	<b>Normal Biodistribution Sample</b> 	<b>Radiopharmaceutical Structure</b> 
<b>Radionuclide</b>	<sup>18</sup> F Half-life 109.7 minutes Emission positron Emax 1.656 MeV	
<b>Molecular Formula and Weight</b>	C <sub>6</sub> H <sub>11</sub> <sup>18</sup> FO <sub>5</sub> 181.1 g atom mole <sup>-1</sup>	
<b>General Tracer Class</b>	Diagnostic PET Radiopharmaceutical.	
<b>Target</b>	Cancer cells, infection, inflammation, viable myocardium, brain Of note: FDG PET/CT is commonly performed for cancer staging and follow-up, evaluation of myocardial viability or sarcoidosis and assessment of neurological conditions including epilepsy and dementia. FDG PET/CT can also be used to assess infection.	
<b>Molecular Process Imaged</b>	Increased glucose metabolism.	
<b>Mechanism for in vivo retention</b>	FDG is a glucose analog that is transported from the blood into cells by glucose transporters (predominantly GLUT1). Once in the cell, FDG is phosphorylated by hexokinase (mainly HK2) to form FDG-6-phosphate. Further metabolism of FDG-6-phosphate is limited and FDG-6-phosphate is essentially trapped in the cell. Although certain cells have phosphatases that dephosphorylate FDG-6-phosphate allowing washout (such as the liver), this is very limited over the imaging time period.	
<b>Metabolism</b>	FDG is phosphorylated in the cell to form FDG-6-phosphate, which is trapped within the cell. FDG is cleared via the kidneys and excreted in the urine.	

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<b>Radiosynthesis</b>	<p><sup>18</sup>F-labeled FDG was first synthesized by Wolf et al. using electrophilic fluorination at Brookhaven National Laboratory in 1976. The idea was to use 3,4,6-tri-O-acetyl-D-glucal as precursor with <sup>18</sup>F-F<sub>2</sub> to produce a 3:1 mixture of <sup>18</sup>F labeled difluoro-glucose and difluoro-mannose derivatives that were then separated and hydrolysed with hydrochloric acid to form 2-fluoro-2-deoxyglucose with a yield of 8% and synthesis time of 2 hours (Ido T, Wan CN, Casella V, et al. "Labeled 2-deoxy-D-glucose analogs: <sup>18</sup>F-labeled 2-deoxy-2-fluoro-D-glucose, 2-deoxy-2-fluoro-D-mannose and <sup>14</sup>C-2-deoxy-2-fluoro-D-glucose". <i>J Labeled Compounds Radiopharm</i> 1978; <b>24</b>: 174–183.)</p> <p>The major limitation of electrophilic fluorination was the low rate of radioactive fluorine incorporation into the precursor agents and production of <sup>18</sup>F-F<sub>2</sub> from a Neon gas target via a <sup>20</sup>Ne(d,α)<sup>18</sup>F reaction. Considerable work has since been done to develop an improved method of radiosynthesis. In 1986, Hamacher <i>et al.</i> reported using Krytox [222]<sup>TM</sup> as a catalyst with a mannose triflate precursor and purification with a series of anion exchange column, C-18 reverse phase column and alumina column to produce <sup>18</sup>F-FDG via nucleophilic fluorination with over 95% purity by a process resulting in yields over 50% and reaction time of approximately 50 minutes. (Hamacher K, Coenen HH, Stocklin G. "Efficient stereospecific synthesis of no-carrier-added 2-[<sup>18</sup>F]-fluoro-2-deoxy-D-glucose using aminopolyether supported nucleophilic substitution". <i>J Nucl Med</i> 1986; <b>27</b>(2): 235-238.)</p> <p>Additional reference: Yu S (2006). "Review of <sup>18</sup>F-FDG synthesis and quality control". <i>Biomed Imaging Interv J</i> 2(4): e57.</p>
<b>Availability</b>	<sup>18</sup> F-FDG has a half-life of under 2 hours, and must be rapidly shipped to its point of use. Many sites manufacture <sup>18</sup> F-FDG using on-site cyclotrons and have developed shipping networks that supply the PET imaging centers in the United States, Canada, Europe and other countries.
<b>Status with USP / EuPh</b>	USP and EuPh monographs have been prepared. USP compliance is described in: SOP 921.01 "Ensuring USP Compliance of <sup>18</sup> F-Fluorodeoxyglucose used in ACRIN studies" The implementation of cGMP for PET by FDA in June of 2012 has led the USP to no longer support monographs for PET radiopharmaceuticals and all FDG synthesis in the United States must be done under FDA through a New Drug Application (NDA), amended New Drug Application (ANDA), investigational new drug application (IND) or an institutional radioactive research drug application (RDRC). All use of FDG that is not clinical must fall under these same FDA rules but implementation for FDG has been delayed and researchers should contact the FDA to be aware of the state of enforcement of the regulations.
<b>Recommended Activity and Allowable mass</b>	<p>According to the practice guidelines for tumor imaging with <sup>18</sup>F-FDG PET/CT available through the Society of Nuclear Medicine and Molecular Imaging website: <a href="http://interactive.snm.org/index.cfm?PageID=772">http://interactive.snm.org/index.cfm?PageID=772</a> and Reves ST, Parisi MT, Gelfand MJ (2011). "Pediatric Radiopharmaceutical Doses: New Guidelines" <i>Radiology</i> <b>261</b>(2): 347-349.</p> <p>The dose for whole-body oncologic PET/CT is typically: 370-740 MBq (10-20 mCi) for adults and 3.7-5.2 MBq/kg (0.1-0.14 mCi/kg) for children.</p> <p>For evaluation of neurologic FDG PET/CT please refer to the practice guidelines available through the Society of Nuclear Medicine and Molecular Imaging website: <a href="http://interactive.snm.org/index.cfm?PageID=772">http://interactive.snm.org/index.cfm?PageID=772</a></p> <p>Additional guidelines are available at: <a href="http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2791475/">http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2791475/</a></p>
<b>Dosimetry</b>	The radiation dose to the patient for <sup>18</sup> F-FDG PET/CT is based on the combination of the radiation dose from the radiopharmaceutical and from the CT portion of the study. The effective dose from the administration of <sup>18</sup> F-FDG for an oncologic PET/CT scan is estimated to be

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	<p>approximately 0.019 mSv/MBq for adults using 370-740 MBq (10-20 mCi). In general, the estimated dose from the radiopharmaceutical is estimated to be 5.2 mSv for a 1-year-old child, 5.9 mSv for a 5-year-old child, 6.6 mSv for a 10-year-old child, 7.3 mSv for a 15-year-old adolescent and 7.4 mSv for an adult. The bladder is the organ receiving the highest radiation dose. The effective dose from the CT portion of the PET/CT study can range from approximately 5 to 80 mSv depending on the CT system and protocol being used but is often comparable to the effective dose from the PET portion of the study.</p> <p>Reference, Society of Nuclear Medicine and Molecular Imaging website: <a href="http://interactive.snm.org/docs/jnm30551_online.pdf">http://interactive.snm.org/docs/jnm30551_online.pdf</a></p> <p>Also, please refer to: Fahey FH, Treves ST, Adelstein SJ (2012). "Minimizing and communicating radiation risk in pediatric nuclear medicine". <i>J Nucl Med Technol</i> <b>40</b>(1): 13-24.</p> <p>The complete reference for FDG dosimetry is Hays M, Watson E, Thomas S, Stabin M. MIRD Dose Estimate Report No. 19: Radiation Absorbed Dose Estimates from <sup>18</sup>F-FDG. <i>J. Nucl Med.</i> 2002; 43:210-214</p>
<b>Pharmacology and Toxicology</b>	There is no definite toxic effect of <sup>18</sup> F-FDG when used as described by the procedure guidelines given by the Society of Nuclear Medicine and Molecular Imaging.
<b>Current Clinical Trials</b>	The NIH clinical trials registry ( <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a> ) should be consulted for a list of current trials using <sup>18</sup> F-FDG. As of early 2013, it listed 772 active or completed clinical trials. Of these, 275 were recruiting subjects.
<b>Reference Site / Person</b>	<p>The FDA describes the development of <sup>18</sup>F-FDG PET on the following site: <a href="http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm182668.htm">http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm182668.htm</a></p> <p>The NCI reports on consensus recommendations for use of <sup>18</sup>F-FDG PET: <a href="http://imaging.cancer.gov/programsandresources/reportsandpublications/publications/clinical-trials-guidelines">http://imaging.cancer.gov/programsandresources/reportsandpublications/publications/clinical-trials-guidelines</a></p>
<b>Imaging Protocol</b>	In general, patients are asked to fast for 4–6 hours prior to the administration of <sup>18</sup> F-FDG. Normally, diabetic patients are asked to fast for 4 hours while non-diabetic patients are asked to fast for 6 hours. Oral hydration prior to and following the study is encouraged. Exercise should be avoided for 24 hours prior to the study. If intravenous contrast material is used, patients should be screened for a history of iodinated contrast material allergy, use of metformin for the treatment of diabetes mellitus and renal disease. Intravenous contrast material should not be administered if serum creatinine is above 2.0 mg/dL. An intraluminal gastrointestinal contrast agent may be used to provide improved imaging of the gastrointestinal tract unless medically contraindicated or unnecessary for the clinical indication. The blood glucose level should be checked before <sup>18</sup> F-FDG administration. Most institutions reschedule the patient if the blood glucose level is greater than 150–200 mg/dL. For brain imaging, the patient should be in a quiet and dimly lit room from the time of radiopharmaceutical administration through the uptake time. For body imaging, a seated or recumbent position is suggested at the time of radiopharmaceutical administration and throughout the uptake phase. For details regarding image acquisition please refer to the Society of Nuclear Medicine and Molecular Imaging website: <a href="http://interactive.snm.org/docs/jnm30551_online.pdf">http://interactive.snm.org/docs/jnm30551_online.pdf</a>
<b>Human Imaging Experience</b>	<p>The first human administration of <sup>18</sup>F-FDG occurred in 1976 in normal volunteers. Listed below are selected references on the use of <sup>18</sup>F-FDG. Either MICAD or PubMed should be searched to find the most recent reports of human imaging studies.</p> <p>Lowe VJ, Fletcher JW, Gobar L, Lawson M, Kirchner P, Valk P, Karis J, Hubner K, Delbeke D, Heiberg EV, Patz EF, Coleman RE. Prospective investigation of positron emission tomography in lung nodules. <i>J Clin Oncol</i> 1998;16:1075-1084.</p> <p>Carr R, Barrington SF, Madan B, O'Doherty MJ, Saunders CAB, van der Walt J, Timothy AR. Detection of lymphoma in bone marrow by</p>

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whole-body positron emission tomography. *Blood* 1998;91:3340-46.

Avril N, Dose J, Janicke F, Sense S, Ziegler S, Laubenbacher C, Romer W, Pache H, Herz M, Allgayer B, Nathrath W, Graeff H, Schwaiger M. Metabolic characterization of breast tumors with positron emission tomography using F-18 fluorodeoxyglucose. *J Clin Oncol* 1996;14:1848-57.

Bury T, Dowlati A, Paulus P, Corhay JL, Hustinx R, Ghaye B, Radermecker M, Rigo R. Whole-body 18-FDG positron emission tomography staging of non-small cell lung cancer. *Eur Respir J* 1997;10:2529-2534.

Delbeke D, Martin WH, Sandler MP, Chapman W, Wright Jr K, Pinson W. Evaluation of benign vs malignant hepatic lesions with positron emission tomography. *Arch Surg* 1998;133:510-516.

Dietlein M, Scheidhauer K, Voth E, Theissen P, Schicha H. Fluorine-18 fluorodeoxyglucose positron emission tomography and iodine-131 whole-body scintigraphy in the follow-up of differentiated thyroid cancer. *Eur J Nucl Med* 1997;24:1342-48.

Friess H, Langhans J, Ebert M, Beger HG, Stollfuss J, Reske SN, Buchler MW. Diagnosis of pancreatic cancer by 2[18-F]-fluoro-2-deoxy-D-glucose positron emission tomography. *Gut* 1995;36:771-777.

Gupta NC, Maloof J, and Gunel E. Probability of malignancy in solitary pulmonary nodules using fluorine-18-FDG and PET. *J Nucl Med* 1996;37:943-948.

Holder Jr. W, White RL, Zuger JH, Easton Jr. EJ, Greene FL. Effectiveness of positron emission tomography for the detection of melanoma metastases. *Annals of Surg* 1998;227:764-771.

Lowe VJ, Hoffman JM, DeLong DM, Patz Jr. EF, Coleman RE. Semiquantitative and visual analysis of FDG-PET images in pulmonary abnormalities. *J Nucl Med* 1994;35:1771-1776.

Moog F, Bangerter M, Kotzerke J, Guhlmann A, Frickhofen N, Reske SN. 18-F-fluorodeoxyglucose-positron emission tomography as a new approach to detect lymphomatous bone marrow. *J Clin Oncol* 1998;16:603-9.

Sazon DA, Santiago SM, Soo Hoo GW, Khonsary A, Brown C, Mandelkern M, Bland W, and Williams AJ. Fluorodeoxyglucose-positron emission tomography in the detection and staging of lung cancer. *Am J Respir Crit Care Med*. 1996;153:417-21.

Schiepers C, Penninckx R, De Vadder N, Merckx E, Mortelmans L, Bormans G, Marchal G, Filez L, Aerts R. Contribution of PET in the diagnosis of recurrent colorectal cancer: comparison with conventional imaging. *Euro J of Surgical Oncology* 1995;21:517-522.

Utech C, Young CS, Winter PF. Prospective evaluation of fluorine-18 fluorodeoxyglucose positron emission tomography in breast cancer for staging of the axilla related to surgery and immunocytochemistry. *Eur J Nucl Med* 1996;23:1588-93.

Valk PE, Pounds TR, Hopkins DM, Haseman MK, Hofer GA, Geiss HB, Myers RW, Lutrin CL. Staging Non-small cell lung cancer by whole-body positron emission tomographic imaging. *Ann Thorac Surg* 1995;60:1573-82.

Vansteenkiste JF, Stroobants SG, De Leyn PR, Dupont PJ, Bogaert J., Maes A, Deneffe GJ, Nackaerts KL, Verschakelen JA, Lerut TE, Mortelmans LA, Demedts MG. Lymph node staging in non-small cell lung cancer with FDG-PET scan: a prospective study of 690 lymph node stations from 68 patients. *J Clin Oncol* 1998;16:2142-2149.

Rudd JH, Warburton EA, Fryer TD, et al. Imaging atherosclerotic plaque inflammation with [18F]-fluorodeoxyglucose positron emission tomography. *Circulation* 2002;105:2708-11.

Rudd JH, Myers KS, Bansilal S, et al. (18)Fluorodeoxyglucose positron emission tomography imaging of atherosclerotic plaque inflammation is highly reproducible: implications for atherosclerosis therapy trials. *J Am Coll Cardiol* 2007;50:892-6.

Rudd JH, Myers KS, Bansilal S, et al. Atherosclerosis inflammation imaging with <sup>18</sup>F-FDG-PET: carotid, iliac, and femoral uptake

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	<p>reproducibility, quantification methods, and recommendations. J Nucl Med 2008;49:871-8.</p> <p>Izquierdo-Garcia D, Davies JR, Graves MJ, et al. Comparison of methods for magnetic resonance-guided [18-f]-fluorodeoxyglucose positron emission tomography in human carotid arteries: reproducibility, partial volume correction, and correlation between methods. Stroke 2009;40:86-93.</p> <p>Padma MV, Said S, Jacobs M, et al. Prediction of pathology and survival by FDG PET in gliomas. J Neurooncol 2003;64:227–237.</p> <p>Di Chiro G. Positron emission tomography using [18F] fluorodeoxyglucose in brain tumors. A powerful diagnostic and prognostic tool. Invest Radiol 1987;22:360–371.</p> <p>Patronas NJ, Di Chiro G, Kufta C, et al. Prediction of survival in glioma patients by means of positron emission tomography. J Neurosurg 1985;62:816–822.</p> <p>Ollenberger GP, Byrne AJ, Berlangieri SU, et al. Assessment of the role of FDG PET in the diagnosis and management of children with refractory epilepsy. Eur J Nucl Med Mol Imaging 2005;32:1311–1316.</p> <p>Kumar A, Juhasz C, Asano E, Sood S, Muzik O, Chugani HT. Objective detection of epileptic foci by 18F-FDG PET in children undergoing epilepsy surgery. J Nucl Med 2010;51:1901–1907.</p> <p>Lewitschnig S, Gedela K, Toby M, et al. 18F-FDG PET/CT in HIV-related central nervous system pathology . Eur J Nucl Med Mol Imaging. 2013 May 18. [Epub ahead of print]</p> <p>O'Doherty MJ, Barrington SF, Campbell M, Lowe J, Bradbeer CS. PET scanning and the human immunodeficiency virus-positive patient. J Nucl Med. 1997;38:1575–83.</p>
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