



Society of Nuclear Medicine 52nd Annual Meeting Highlights of the Society of Nuclear Medicine 52nd Annual Meeting CME

Complete author [affiliations and disclosures](#) are at the end of this activity.

The materials presented here were prepared by independent authors under the editorial supervision of Medscape and do not represent a publication of the Society of Nuclear Medicine. These materials and the related activity are not sanctioned by the Society of Nuclear Medicine or the commercial supporter of the conference, and do not constitute an official part of that conference.

Release Date: August 22, 2005; Valid for credit through August 22, 2006

Target Audience

This activity is intended for radiologists, nuclear medicine specialists, and select referring physicians (cardiologists, oncologists, pediatric specialists, and other relevant specialty physicians) with an interest in integrating advanced imaging techniques, such as PET scanning, PET-CT fusion, molecular imaging, and immunodiagnostics and immunotherapeutics, into their practice to facilitate the early detection and clinical management of cardiac disease, cancer, pediatric malignancies, and other disease entities that are amenable to PET/PET-CT fusion diagnosis.

Goal

The objective of this activity is to spotlight the clinical utility of advanced imaging studies, such as PET scanning, PET-CT fusion, and molecular imaging, in the detection and treatment of early disease; define appropriate settings for the use of this technology; and offer a venue for an expert in this facet of imaging to outline the value of these technologies for the radiology, nuclear medicine, oncology, cardiology, and pediatric specialist as well as other relevant clinical audiences on Medscape.

Learning Objectives for this CME Activity

Upon completion of this activity, participants will be able to:

1. Denote the appropriate use of various imaging modalities, including PET, CT, and SPECT, in the accurate assessment of cardiac disease.
2. Define the emerging role of radioimmunotherapy in the effective management of cancer.
3. Discuss the value of radioimmunotherapy in the treatment of lymphoma.
4. Describe the role of biomarkers in molecular medicine as predictors of potential toxicity and as benchmarks to determine patient prognosis.
5. Detail the utility of PET scanning and PET-CT fusion studies in refining the management of pediatric brain tumors, Hodgkin's lymphoma, and inflammatory bowel disease.

Credits Available

Physicians - up to 0.75 AMA PRA Category 1 continuing physician education credits

All other healthcare professionals completing continuing education credit for this activity will be issued a certificate of participation.

Participants should claim only the number of hours actually spent in completing the educational activity.

Accreditation Statements

For Physicians



Medscape is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Medscape designates this educational activity for a maximum of **0.75 Category 1 credit(s)** toward the AMA Physician's Recognition Award. Each physician should claim only those credits that reflect the time he/she actually spent in the activity.

For questions regarding the content of this activity, contact the accredited provider for this CME/CE activity: CME@webmd.net. For technical assistance, contact CME@webmd.net.

This activity is supported by funding from WebMD.



Instructions for Credit

There are no fees for participating in or receiving credit for this online educational activity. For information on applicability and acceptance of continuing education credit for this activity, please consult your professional licensing board.

This activity is designed to be completed within the time designated on the title page; physicians should claim only those credits that reflect the time actually spent in the activity. To successfully earn credit, participants must complete the activity online during the valid credit period that is noted on the title page.

Follow these steps to earn CME/CE credit*:

1. Read the target audience, learning objectives, and author disclosures.
2. Study the educational content online or printed out.
3. Online, choose the best answer to each test question. To receive a certificate, you must receive a passing score as designated at the top of the test. Medscape encourages you to complete the Activity Evaluation to provide feedback for future programming.

You may now view or print the certificate from your CME/CE Tracker. You may print the certificate but you cannot alter it. Credits will be tallied in your CME/CE Tracker and archived for 5 years; at any point within this time period you can print out the tally as well as the certificates by accessing "Edit Your Profile" at the top of your Medscape homepage.

*The credit that you receive is based on your user profile.

Legal Disclaimer

The materials presented here do not reflect the views of Medscape or the companies providing unrestricted educational grants. These materials may discuss uses and dosages for therapeutic products that have not been approved by the United States Food and Drug Administration. A qualified healthcare professional should be consulted before using any therapeutic product discussed. All readers or continuing education participants should verify all information and data before treating patients or employing any therapies described in this educational activity.

Copyright © 2005 Medscape.

Contents of This CME Activity

1. [PET and PET-CT: Expanding the Scope of Cardiovascular Imaging](#)
Hossein Jadvar, MD, PhD

2. [Immunodiagnostics Shape Immunotherapeutics for Improved Cancer Care](#)
Hossein Jadvar, MD, PhD
3. [Molecular Imaging Update: "Personalized" Imaging for Improved Diagnosis and Treatment Decisions](#)
Hossein Jadvar, MD, PhD
4. [Refining Pediatric Cancer Management Through PET and PET-CT](#)
Hossein Jadvar, MD, PhD

PET and PET-CT: Expanding the Scope of Cardiovascular Imaging

Hossein Jadvar, MD, PhD

Positron emission tomography (PET) has been important in cardiovascular research and in clinical cardiology. Although numerous radiopharmaceuticals have been used to render physiologic, biochemical, and clinical information, [F-18]-fluorodeoxyglucose (FDG) imaging is the most common, which is used for identification of jeopardized but viable myocardium that can be salvaged with revascularization. Myocardial perfusion imaging with PET agents provides higher resolution than single photon emission computed tomography (SPECT) agents, and PET agents can be used to determine absolute blood flow. Rubidium-82, used for myocardial perfusion imaging, was the first PET agent approved by the US Food and Drug Administration. PET myocardial perfusion imaging, especially quantitative myocardial perfusion imaging, has proven clinical value. However, imaging with SPECT is likely to remain the dominant method for myocardial perfusion imaging in most circumstances, because it is less expensive to perform.^[1-10]

The expanding role of cardiac PET and PET-computed tomography (CT) was highlighted at the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada, by several categoric seminars and scientific sessions. In a well-attended symposium entitled "Role of SPECT, Coronary CT, and PET/CT in the Diagnosis and Management of CAD," 3 seasoned speakers provided a review of the literature and included their own opinions regarding what the future of cardiac imaging may hold. Jack Ziffer, MD, from the Baptist Cardiac & Vascular Institute in Miami, Florida, attempted to pursue the audience that cardiac CT will be the dominant method to evaluate patients with suspected coronary artery disease (CAD), because CT can provide combined information on morphology, function, perfusion, viability, coronary anatomy, and coronary calcium (which is a preclinical indicator of CAD). Daniel Berman, MD, from Cedars-Sinai Medical Center in Los Angeles, California, contrasted Dr. Ziffer's comments by arguing that there will be paradigm shifts in cardiac diagnosis and therapy from the current assessment of risk factors to the more robust assessment of specific markers of subclinical disease. Dr. Berman believes that myocardial perfusion SPECT and coronary calcium CT scoring will be sufficient for most clinical imaging needs. In particular, it was suggested that because the amount of calcified plaques predicts the total coronary plaque burden, healthy men older than 45 years and healthy women older than 55 years may consider undergoing cardiac CT for coronary calcium scoring. If the calcium score is greater than 400, then additional myocardial perfusion SPECT imaging will detect subclinical ischemia in 10% to 20% of these individuals, which allows for early intervention. The session concluded by additional closing remarks and review of the clinical utility of PET by Dr. Marcelo Di Carli, MD, from the Brigham and Women's Hospital in Boston, Massachusetts.^[11]

New Options Span Several Modalities

In a scientific session entitled "Advances in Cardiac PET and PET-CT," several investigators presented data on both the technical and the clinical aspects of these imaging modalities. DiFilippo and colleagues^[12] showed that the PET metal-related artifact due to the CT attenuation correction procedure was only significant with the implantable cardioverter-defibrillator leads and not with the other type of pacing leads. The artifacts from implanted leads in cardiac PET-CT may also be reduced with compensatory techniques that were reported by a group from Kansas City, Missouri.^[13]

Lu and coworkers,^[14] from Montefiore Medical Center in New York, NY, showed that additional evaluation with rubidium-82 myocardial perfusion PET scan can be useful in a subset of women with equivocal sestamibi myocardial perfusion SPECT studies, because PET demonstrates unequivocal normal perfusion in as much as 77% of these patients. PET was also shown to be useful to assessing the endotheliopathy associated with primary antiphospholipid syndrome. During pharmacologic stress with dipyridamole or adenosine stress, coronary vessels respond with an endothelial-mediated and smooth muscle-mediated vasodilation. The endothelial-dependent vasodilation index can also be assessed with a cold pressor test (performed by immersing 1 hand in cold water). With a 3-phase (rest-cold

pressor test stress) PET protocol and 30 mCi of radiolabeled ammonia for each phase, Alexanderson and colleagues,^[15] from Mexico, showed that patients with antiphospholipid syndrome have low coronary flow reserve and an endothelial-dependent vasodilation index. In another study with ammonia PET scans performed at rest, with dipyridamole stress, and 1 hour after stress, investigators from Japan showed that the global myocardial hyperemic effect of dipyridamole was almost normalized 1 hour after the stress test. However, in some cases, delayed dipyridamole-induced vascular response persisted on the ischemic myocardium, suggesting that the usual time of imaging with technetium agents 1 hour after stress is not a true resting condition.^[16]

The investigators from The Cleveland Clinic, Cleveland, Ohio, reported on the impact of a "slow" CT transmission scan, acquired over several respiratory cycles (42 seconds) for attenuation correction, on the measurements of left ventricular function derived from gated cardiac PET images.^[17] The left ventricular ejection fraction obtained from magnetic resonance imaging (MRI) was used as the standard of reference for comparison. The results indicated that left ventricular ejection fraction values derived from gated cardiac PET-CT images corrected for attenuation with the slow CT technique are feasible for routine clinical use.

FDG PET is considered an accurate diagnostic imaging test for assessing myocardial viability when compared with functional improvement after revascularization as the standard of reference. A study from Japan also reported on the diagnostic utility of C-11 choline in this clinical setting.^[18] Choline is a component of phosphatidylcholine, which is an essential element of the cellular membrane phospholipids. Loss of cellular viability has been shown to be associated with the loss of the phosphatidylcholine molecule. For this reason, viable myocardium would be expected to demonstrate high C-11 choline uptake on PET. The sensitivity, specificity, and accuracy of C-11 choline were found to be 60%, 100%, and 66% when greater than 55% of the FDG percentage of uptake was considered as the threshold for predicting viability.^[18]

The clinical applications of cardiac PET and PET-CT will likely expand as nuclear molecular imaging shifts from the current single-photon-based, nonquantitative imaging systems to the more sophisticated positron-based, quantitative hybrid structural-functional imaging systems.

References

1. Barrington SF, Chambers J, Hallett WA, et al. Comparison of sestamibi, thallium, echocardiography and PET for the detection of hibernating myocardium. *Eur J Nucl Med Mol Imaging*. 2004;31:355-361. [Abstract](#)
2. Jadvar H, Strauss HW, Segall GM. SPECT and PET in the evaluation of coronary artery disease. *Radiographics*. 1999;19:915-926. [Abstract](#)
3. Parker JA. Cardiac nuclear medicine in monitoring patients with coronary heart disease. *Semin Nucl Med*. 2001;31:223-237. [Abstract](#)
4. Rudd JH, Warburton EA, Fryer TD, et al. Imaging atherosclerotic plaque inflammation with [18F]-fluorodeoxyglucose positron emission tomography. *Circulation*. 2002;105:2708-2711. [Abstract](#)
5. Schelbert HR, Phelps ME, Huang SC, et al. N-13 ammonia as an indicator of myocardial blood flow. *Circulation*. 1981;63:1259-1272. [Abstract](#)
6. Schindler TH, Nitzsche EU, Olschewski M, et al. PET-measured responses of MBF to cold pressor testing correlate with indices of coronary vasomotion on quantitative coronary angiography. *J Nucl Med*. 2004;45:419-428. [Abstract](#)
7. Strauss HW, Grewal RK, Pandit-Taskar N. Molecular imaging in nuclear cardiology. *Semin Nucl Med*. 2004;34:47-55. [Abstract](#)
8. Tillisch J, Brunken R, Marshall R, et al. Reversibility of cardiac wall-motion abnormalities predicted by positron tomography. *N Engl J Med*. 1986;314:884-888. [Abstract](#)
9. Wyss CA, Koepfli P, Mikolajczyk K, et al. Bicycle exercise stress in PET for assessment of coronary flow reserve: repeatability and comparison with adenosine stress. *J Nucl Med*. 2003;44:146-154. [Abstract](#)
10. Yokoyama I, Yonekura K, Ohtake T, et al. Role of insulin resistance in heart and skeletal muscle F-18 fluorodeoxyglucose uptake in patients with non-insulin-dependent diabetes mellitus. *J Nucl Cardiol*. 2000;7:242-248. [Abstract](#)
11. Categorical seminar: "role of SPECT, coronary CT, and PET/CT in the diagnosis and management of CAD." Di Carli M (organizer). Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada.
12. DiFilippo FP, Brunken RC, Bybel B, Hamil JJ. Clinical significance of metal artifact reduction in cardiac PET-CT. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. *J Nucl Med*. 2005;46(suppl2):115P. Abstract 330.
13. Hsu BL, Moser KW, Cullom SJ, Bateman TM, Helmuth PA, Case JA. Correction of imaging artifacts from implanted leads in cardiac PET/CT: a phantom evaluation. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. *J Nucl Med*. 2005;46

- (suppl2):174P. Abstract 500.
14. Lu P, Milstein D, Valdivia A, et al. Diagnostic value of rubidium-82 myocardial perfusion PET in women with equivocal Tc-99m-sestamibi gated myocardial perfusion SPECT. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. J Nucl Med. 2005;46(suppl2):115P. Abstract 332.
 15. Alexanderson E, Ricalde A, Vargas A, Meave A, Amigo MI. Reduction in coronary flow reserve determined by positron emission tomography in primary antiphospholipid syndrome: a case controlled study. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. J Nucl Med. 2005;46(suppl2):116P. Abstract 333.
 16. Kudo T, Hata T, Yamauchi H, et al. Abnormal distribution of myocardial perfusion does not normalize 1 hour after dipyridamole stress test: evaluation with N-13 ammonia PET. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. J Nucl Med. 2005;46(suppl2):116P. Abstract 335.
 17. Brunken RC, DiFilippo FP, Howe WC, Baker MT, White RD, Stillman AE. Measurement of left ventricular ejection fraction using gated cardiac PET with CT based attenuation correction. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. J Nucl Med. 2005;46(suppl2):173P. Abstract 499.
 18. Takahashi N, Inoue T, Oka T, Lee J, Umemura S. Viability assessment in patients with myocardial infarction by C-11 choline PET. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. J Nucl Med. 2005;46(suppl2):117P. Abstract 336.
-

Immunodiagnostics Shape Immunotherapeutics for Improved Cancer Care

Hossein Jadvar, MD, PhD

There is rapid emergence of recombinant and antibody-based reagents, which specifically target biomarkers of disease. Radiolabeling of antibodies has provided the means for cancer imaging and therapy. Recent US Food and Drug Administration (FDA) approval of rituximab, gemtuzumab ozogamicin, alemtuzumab, and ibritumomab tiuxetan for cancer radioimmunotherapy has fueled the further expansion of immunodiagnosis and immunotherapy. Among the monoclonal antibodies (mAb), anti-CD20 mAbs have been most extensively investigated and have shown definitive clinical efficacy. Rituximab is a genetically engineered chimeric anti-CD20 mAb, with mouse variable and human constant regions. Clinical trials have revealed that rituximab is a highly effective agent with acceptable toxicities against indolent and aggressive B-cell non-Hodgkin's lymphomas -- either as a single agent or in combination with chemotherapy. Radioimmunotherapy uses the mAb to target radiation to lymphoma tissue while minimizing toxicity to normal cells. The clinical trials of beta-emitting Y-90 ibritumomab tiuxetan (*Zevalin*; IDEC Pharmaceuticals Corporation, San Diego, California) and I-131 tositumomab (*Bexxar*; GlaxoSmithKline, Philadelphia, Pennsylvania) have shown efficacy in relapsed B-cell non-Hodgkin's lymphomas with acceptable toxicities. Radioimmunotherapy has also facilitated a team approach to patient management by capitalizing on building relationships between oncologists and nuclear medicine physicians.^[1-10]

The importance of radioimmunotherapy was visibly highlighted at the Society of Nuclear Medicine 52nd Annual Meeting on June 18-22, 2005, in Toronto, Ontario, Canada. There were scientific sessions dedicated to this technology as well as presentations by industry.

Delineating Cancer Before It Is Cancer

Immunodiagnosis was the topic of a scientific session that summarized the recent studies on the design and testing of various antibodies. Van Schaijk and colleagues^[11] presented the development of a pretargeting strategy for carcinoembryonic antigen (CEA)-expressing tumors with a new bispecific mAb. The investigators demonstrated very high tumor-to-background ratios with this agent due to its high specificity and rapid background clearance. The same group of investigators also reported a similar strategy with bispecific antibodies for pretargeting of renal cell carcinoma.^[12] Goldenberg and associates^[13] evaluated the radiolabeled bispecific pretargeting system with dynamic imaging. It was demonstrated that a bispecific pretargeting system is superior to directly radiolabeling antibody targeting methods due to an increase in the signal-to-background ratio. In another report from The Netherlands, the results of a radiolabeled anti-P-glycoprotein (Pgp) antibody were discussed.^[14] Pgp is a membrane efflux pump

protein that is upregulated in some tumors. Pgp is associated with multidrug resistance and poor response to several chemotherapeutics. The study authors argued that in vivo targeting and visualization of Pgp provide knowledge about multidrug resistance prior to treatment. Their animal studies in nude mice bearing human uterus sarcoma cells with either high- or low-Pgp expression showed an average of 7.8% higher radioactivity concentration in the high-Pgp-expressing tumors. Another study from the University of California, Los Angeles, and the City of Hope National Medical Center in Duarte, California, reported on the use of micropositron emission tomography (PET) to evaluate copper-64-labeled antibody fragments in HER-2 and CEA tumor antigen systems.^[15] In the CEA system, the antibody fragment demonstrated excellent targeting. However, for the HER-2 system, an increase of the minibody size was necessary to enhance targeting, suggesting that microPET imaging may be helpful for tailoring the antibody fragment-targeting properties.

Update on Radioimmunotherapy Innovations for Treating Malignancies

Radioimmunotherapy is a promising treatment modality for cancer. There were several studies that presented data on the emerging role of immunotherapy. Chung and colleagues,^[16] from South Korea, showed that Re-188-labeled 3E8 antibody (an affinity-improved anti-TAG-72 antibody against TAG-72 antigen, which is expressed by many human adenocarcinomas) suppressed tumor growth temporarily. In another animal study with implanted ovarian tumors with high HER-2/*neu* antigen expression, the antitumor effect of trastuzumab (*Herceptin*) was shown to be enhanced by radiolabeling the antibody with the alpha emitter At-211.^[17] Fischer and coworkers,^[18] from Germany, also presented their initial biokinetic data on a new promising immunotherapy for neuroblastoma. They radiolabeled an antibody directed against the neural crest adhesion molecule, which is expressed highly on nearly all neuroblastoma cells. The efficacy of radioimmunotherapy may be improved by pretargeting. Such a strategy was tested for radioimmunotherapy of colon cancer, which showed that pretargeting with a trivalent bispecific mAb improves antitumor responses when compared with a directly radiolabeled antibody administered at equitoxic doses.^[19] In another study, radioimmunotherapy was combined with antiangiogenic therapy. In this strategy, it was noted that in a mouse model of medullary thyroid cancer, pretreatment with an antiangiogenic drug (thalidomide or cyclopeptidic vascular endothelial growth inhibitor) improved the efficacy of the anti-CEA 131I-F6 mAb radioimmunotherapy with an acceptable toxicity.^[20]

Several studies reported on the radioimmunotherapy of lymphoma. Chatal and colleagues^[21] reported on the encouraging results of the safety and efficacy of an ongoing phase 1-2, multicenter, dose-escalation trial on humanized anti-CD22 epratuzumab radiolabeled with Y-90. Zwas and associates,^[22] from Israel, showed that use of Y-90-ibritumomab tiuxetan in a stem cell transplantation-conditioning regimen is relatively safe and may improve outcome in severe refractory non-Hodgkin's lymphoma. The favorable results of an Australian study on I-131 rituximab radioimmunotherapy in non-Hodgkin's lymphoma were the subject of another report, which indicated the potential for efficacious repeat treatments upon relapse.^[23] The Swiss reported on the phase 1-2 results of Lu-177 rituximab (anti-CD20) for treatment of relapsed lymphoma, which demonstrated that this regimen is well tolerated and effective.^[24] Conti and colleagues,^[25] from the University of Southern California in Los Angeles, California, reported the results of the Zevalin Image Registry. The study authors noted that of more than 600 patients in clinical trials prior to market launch, only 1 patient did not receive Y-90 ibritumomab tiuxetan because of altered biodistribution. Of the 953 patients treated within 1 year of market launch, fewer than .7% were precluded from radioimmunotherapy due to altered biodistribution. The first In-111 ibritumomab tiuxetan scan detected all the rare cases of altered biodistribution, suggesting that the typical second scan and potentially a third scan may be unnecessary -- leading to simplification of the treatment procedure.^[25]

The future of radioimmunotherapy appears to be bright as we continue to witness the development of new, radiolabeled, immune-based agents for the treatment of cancer and other diseases.

References

1. Conti PS. The future of radioimmunotherapy: a PET perspective. *Semin Oncol.* 2005;32(suppl1):S63-S67.
2. Davies AJ. A review of tositumomab and I(131) tositumomab radioimmunotherapy for the treatment of follicular lymphoma. *Expert Opin Biol Ther.* 2005;5:577-588. [Abstract](#)
3. Emmanouilides C. Radioimmunotherapy for non-Hodgkin's lymphoma. *Semin Oncol.* 2003;30:531-544. [Abstract](#)
4. Fink-Bennett DM, Thomas K. 90Y-ibritumomab tiuxetan in the treatment of relapsed or refractory B-cell non-Hodgkin's lymphoma. *J Nucl Med Technol.* 2003;31:61-68. [Abstract](#)
5. Krasner C, Joyce RM. Zevalin: 90yttrium labeled anti-CD20 (ibritumomab tiuxetan), a new treatment for non-Hodgkin's lymphoma. *Curr Pharm Biotechnol.* 2001;2:341-349. [Abstract](#)
6. Hudson PJ, Souriau C. Recombinant antibodies for cancer diagnosis and therapy. *Expert Opin Biol Ther.*

- 2003;3:305-318. [Abstract](#)
7. Spies SM. Imaging and dosing in radioimmunotherapy with yttrium 90 ibritumomab tiuxetan (Zevalin). *Semin Nucl Med.* 2004;34(suppl1):10-13.
 8. Tobinai K. Rituximab and other emerging monoclonal antibody therapies for lymphoma. *Expert Opin Emerg Drugs.* 2002;7:289-302. [Abstract](#)
 9. Verel I, Visser GW, van Dongen GA. The promise of immuno-PET in radioimmunotherapy. *J Nucl Med.* 2005;46(suppl1):164S-171S.
 10. Wiseman GA, Kornmehl E, Leigh B, et al. Radiation dosimetry results and safety correlations from 90Y-ibritumomab tiuxetan radioimmunotherapy for relapsed or refractory non-Hodgkin's lymphoma: combined data from 4 clinical trials. *J Nucl Med.* 2003;44:465-474. [Abstract](#)
 11. van Schaijk F, Frielink C, McBride WJ, et al. Pretargeting of CEA-expressing tumors with biologically produced bispecific anti-CEA X anti-DTPA bispecific antibodies. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 428.
 12. van Schaijk F, Soede A, McBride WJ, et al. Pretargeting of renal cell carcinoma: use of residualizing iodine and use of intact or fragmented bispecific antibodies. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 429.
 13. Goldenberg DM, Sharkey RM, Cardillo TM, et al. Signal amplification in molecular imaging by pretargeting with a new multivalent bispecific nanobody (bsNAb). Pretargeting of renal cell carcinoma: use of residualizing iodine and use of intact or fragmented bispecific antibodies. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 431.
 14. van Eerd JE, Soede A, Corstens FH, Oyen WJ, Boerman OC. Targeting of PGP-expressing tumors with a radiolabeled anti-PGP antibody. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 432.
 15. Olafsen T, Kenanova VE, Gambhir SS, Raubitschek AA, Shively JE, Wu AM. MicroPET evaluation of Cu-64-labeled antibody fragments (minibody vs. scFv-Fc) in two tumor antigen systems (HER2 and CEA). Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 433.
 16. Chung HK, Choi TH, Hong HJ, et al. Therapeutic effect of 188Re labeled humanized anti-TAG72 antibody in LS174T tumor bearing nude mice. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 414.
 17. Palm S, Andersson H, Back T, et al. Alpha-particle emitter astatine-211-mediated anticancer efficiency of trastuzumab (Herceptin): single-dose and fractionated therapy with 211At-Herceptin in a nude mouse ovarian carcinoma. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 415.
 18. Fischer T, Otto C, Jensen M, et al. I-131-ERIC-antibody for neuroblastoma therapy: first biokinetic data. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 416.
 19. Karacay H, Sharkey RM, Rossi EA, et al. Improved radioimmunotherapy of human colon cancer xenografts by pretargeting with a new trivalent, bisppecific monoclonal antibody (bsMAb) and 90Y-labeled peptide. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 418.
 20. Kraeber-Bodere F, Sai-Maurel C, Faivre-Chauvet A, et al. Toxicity and efficacy of combined radioimmunotherapy and antiangiogenic therapy in mouse model of medullary thyroid carcinoma. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 420.
 21. Chatal JF, Harousseau JL, Griesinger F, et al. Fractionated radioimmunotherapy in NHL with DOTA-conjugated, humanized anti-CD22 epratuzumab at high cumulative 90Y doses. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 447.
 22. Zwas TS, Shimoni A, Oksman Y, Goshen E, Kamchi M, Nagler A. Zevalin treatment in conditioning regimens for stem cell transplantation in non-Hodgkin's lymphoma. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 442.
 23. Turner H, Hicks RJ, Seymour JF, Leahy MF. 131I-rituximab radioimmunotherapy in relapsed/refractory indolent non-Hodgkin's lymphoma: phase II multicenter Australian clinical study. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 444.
 24. Forrer F, Lohri A, Schmid P, Hermann R, Maecke HR, Muller-Brand J. Radioimmunotherapy with lutetium-177-DOTA-rituximab: a phase I/II study. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 445.
 25. Conti PS, White CA, Pieslor PC, et al. A single indium-111 imaging scan reliably captures rare instances of altered biodistribution of ibritumomab tiuxetan (Zevalin): results from the Zevalin Imaging Registry. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 441.

Molecular Imaging Update: "Personalized" Imaging for Improved Diagnosis and Treatment Decisions

Hossein Jadvar, MD, PhD

Molecular imaging is emerging as an important research tool in the way that we study cellular and molecular events in vivo, and it is expected to lead radiology into the forefront of molecular and clinical medicine. Molecular imaging is the product of concurrent advances in molecular and cellular biology, chemistry, computing, and imaging science. It refers to the multidisciplinary techniques that are involved in remote sensing, characterization, and measurement of cellular events in vivo at the molecular level in health and disease. Molecular imaging will pave the way in the evolution from the current, nonspecific imaging methods toward patient-specific imaging evaluation based on morphologic, physiologic, molecular, and genetic markers of disease. This important task will be achieved through the use of multimodality imaging systems and "smart" specific imaging agents in achieving the key tasks of accurate diagnosis, treatment evaluation, surveillance, and prognosis in individual patients.^[1-48]

As typical of recent, major medical imaging scientific meetings, the importance of molecular imaging was again visibly highlighted at the Society of Nuclear Medicine (SNM) 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada, by several, well-attended invited lectures and scientific sessions.^[49-60] The formal opening of the SNM meeting this year was the Henry Wagner Plenary Session, which was delivered by Sanjiv Sam Gambhir, MD, PhD,^[49] Director of Molecular Imaging, Stanford University, Stanford, California. Dr. Gambhir noted that the current revolutionary changes are occurring through a merge of molecular and cellular biology, medical imaging, pharmacology, systems biology, and nanotechnology, which focus on the development of novel approaches to molecular diagnostics and therapeutics. Dr. Gambhir reviewed the major imaging modalities and strategies that allow in vivo repeated imaging of fundamental cellular events. These imaging modalities are available for studying small animals in order to facilitate translational research with various imaging biomarkers. Small-animal imaging systems, such as micropositron emission tomography (PET), microsingle photon emission computed tomography (SPECT), microcomputed tomography (CT), optical cameras, and ultrasound, are commercially available. The pharmaceutical industry has already embraced small-animal molecular imaging for the cost-effective, rapid development and testing of drugs. Dr. Gambhir reviewed the current research efforts on molecular imaging and noted that the concept of molecular imaging, regardless of the imaging modality and type of imaging reporter agent, has always been the mainstay of nuclear medicine. He concluded that nuclear medicine will continue to be the champion for molecular imaging research, which is expected to propel us into a new environment of imaging-based, personalized molecular diagnostics and therapeutics.

Diverse Molecular Imaging Applications Spotlight Value

At the 2005 SNM meeting, there was also a well-attended review session entitled "Molecular Imaging 101" that summarized the current research and potential clinical applications of molecular imaging.^[50] The session emphasized the role of imaging biomarkers in clinical trial design. A suitable imaging biomarker can reduce the cost of drug discovery and development by providing an objectively measured indicator for changes in the biological processes in response to therapy. In fact, an imaging biomarker may be developed that can substitute for clinical end points. This imaging biomarker-based surrogate end point will be able to predict harm or benefit from therapy, and thereby reduce the number of patients needed in clinical drug trials by optimizing response rate and decreasing cost and unnecessary drug toxicity. The pivotal importance of this new strategy becomes clear when one notes that the development of a drug from concept to clinical testing in people may take more than a decade at a cost of more than \$1 billion.

There were also several scientific sessions dedicated to the development and testing of biomarkers in molecular imaging with titles, such as "Monitoring of Gene Therapy," "Visualization of Tumor Hypoxia," and "Identification and Evaluation of New Tracer Molecules." Penuelas and colleagues^[51] reported that PET imaging with [F-18]-FHBG (fluorohydroxymethylbutyl-guanine) may be useful for monitoring transgene expression in patients with hepatocellular carcinoma after ultrasound-guided direct intratumoral injection of a recombinant adenovirus encoding the *HSV1-tk* (herpes simplex virus type 1-thymidine kinase) gene driven by the cytomegalovirus promoter. Similar findings with microPET imaging in mice were reported by Kuruppu and associates,^[52] from Massachusetts General Hospital in

Boston, Massachusetts. These studies suggested the potential use of PET imaging for monitoring clinical trials of gene therapy in cancer. Alauddin and coworkers,^[53] from the University of Southern California in Los Angeles, California, compared several F-18-labeled pyrimidine nucleoside analogs (FFAU, FCAU, FBAU, FIAU, FMAU, and FEAU) as potential radiotracers for *HSV1-tk* gene expression in human breast cancer. In vitro results showed that although FFAU, FEAU, and FIAU can all be used to visualize suicide gene expression in human breast cancer, similar to the investigators' results in human colon cancer, FEAU was superior in terms of imaging sensitivity and specificity in transduced breast cancer cells. These studies reinforce the notion that it will soon be possible to image human gene therapy to assess the location, amplitude, extent, and duration of gene expression.

Several studies also reported on the use of PET in imaging hypoxia. It is recognized that tumor hypoxia leads to genetic changes that promote aggressive tumor phenotype and resistance to both chemotherapy and radiation therapy. Rajendran and colleagues,^[54] from the University of Washington, Seattle, showed that PET imaging with [F-18]-fluoromisonidazole (FMISO) was useful to characterize and quantify hypoxia in human cervical cancer. Such information may therefore be helpful for improved prediction of therapy response and potential early application of more aggressive therapeutic interventions in hypoxic tumors. Pugachev and associates,^[55] from the Memorial Sloan-Kettering Cancer Center in New York, NY, also reported on validation of a tumor model containing a hypoxia-inducible reporter gene by measuring [F-18]-FMISO uptake in the tumor. Two investigations of hypoxia imaging with PET included abstracts on the use of [F-18]-fluoroazomycin arabinoside (FAZA). These studies included investigations on human head and neck cancer^[56] and prediction of success of radiation therapy.^[57] Beck and associates^[58] also demonstrated that the spatial distribution and expression of the *HIF-1 alpha* (hypoxia-inducible factor 1 alpha) gene correlated significantly with tumor hypoxia, as assessed by FAZA uptake in the tumor.

In 2 studies from Germany, tumor glucose metabolism, as assessed by the level and distribution of [F-18]-fluorodeoxyglucose (FDG) uptake, was correlated with the expression of various genes with a gene chip.^[59,60] It was noted that overall FDG uptake can be increased shortly after therapy, which may be related to cell-repair functions.^[59] The same German investigators also used the combined evaluations of FDG PET imaging data and the gene chip data for detecting possible targets for the development of new specific radiotracers in tumor diagnostics.^[60] Jadvar and colleagues^[61] also reported on the microPET imaging study of the glucose metabolism in human prostate tumors implanted in mice. The biologically more aggressive androgen-independent tumors demonstrated more rapid growth patterns and higher glucose metabolism than those in androgen-sensitive tumors. This preclinical observation suggested that FDG PET may have a clinical role in the early prediction of the hormone-refractory state, which then may be important in early deliverance of therapeutic intervention and potential improvement in outcome.

The ever-increasing visibility of molecular imaging research, as exemplified at the 2005 SNM meeting, reinforces the notions that molecular imaging will change the current practice of clinical medicine and is expected to bring together physicians and scientists facilitating interdisciplinary research and development for the betterment of the human condition.

References

1. Benaron DA. The future of cancer imaging. *Cancer Metastasis Rev.* 2002;21:45-78. [Abstract](#)
2. Blasberg RG, Gelovani (Tjuvajev) J. Molecular-genetic imaging: a nuclear medicine-based perspective. *Mol Imag.* 2002;1:280-300.
3. Blasberg RG, Gelovani-Tjuvajev J. In vivo molecular-genetic imaging. *J Cell Biochem Suppl.* 2002;39:172-183. [Abstract](#)
4. Blasberg RG. Molecular imaging and cancer. *Mol Cancer Ther.* 2003;2:335-343. [Abstract](#)
5. Brindle KM. Molecular imaging using magnetic resonance: new tools for the development of tumor therapy. *Br J Radiol.* 2003;76(suppl2):S111-S117.
6. Britz-Cunningham SH, Adelstein SJ. Molecular targeting with radionuclides: state of science. *J Nucl Med.* 2003;44:1945-1961. [Abstract](#)
7. Chatziioannou AF. PET scanners dedicated to molecular imaging of small animal models. *Mol Imaging Biol.* 2002;4:47-63. [Abstract](#)
8. Cherry SR. In vivo molecular and genomic imaging: new challenges for imaging physics. *Phys Med Biol.* 2004;49:R13-48. [Abstract](#)
9. Choy G, Choyke P, Libutti SK. Current advances in molecular imaging: noninvasive in vivo bioluminescent and fluorescent optical imaging in cancer research. *Mol Imaging.* 2003;2:303-312. [Abstract](#)
10. Danthi SN, Pandit SD, Li KC. A primer on molecular biology for imagers VII. Molecular imaging probes. *Acad Radiol.* 2004;11(suppl):77-84.
11. Doubrovin M, Serganova I, Mayer-Kuckuk P, et al. Multimodality in vivo molecular-genetic imaging. *Bioconjug Chem.* 2004;15:1376-1388. [Abstract](#)

12. Gambhir SS. Molecular imaging of cancer with positron emission tomography. *Nat Rev Cancer*. 2002;2:683-693. [Abstract](#)
13. Gambhir SS. Molecular imaging of cancer with positron emission tomography. *Nat Rev Cancer*. 2002;2:683-693. [Abstract](#)
14. Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell*. 2000;100:57-70. [Abstract](#)
15. Heath JR, Phelps ME, Hood L. Nanosystems biology. *Mol Imag Biol*. 2003;5:312-325.
16. Hildebrandt IJ, Gambhir SS. Molecular imaging applications for immunology. *Clin Immunol*. 2004;111:210-224. [Abstract](#)
17. Hoffman JM, Menkens AE. Molecular imaging in cancer: future directions and goals of the National Cancer Institute. *Acad Radiol*. 2000;7:905-907. [Abstract](#)
18. Jadvar H, Conti PS. Molecular imaging: frontier of molecular medicine and imaging science. In: Alizadeh BN, ed. *Biotechnology International III*. San Francisco, Calif: Universal Medical Press Inc.; 2001:293-298.
19. Li KC, Pandit SD, Guccione S, Bednarski MD. Molecular imaging applications in nanomedicine. *Biomed Microdevices*. 2004;6:113-116. [Abstract](#)
20. Li KC. Molecular imaging: opportunities and challenges for bioengineers. Why is molecular imaging receiving so much attention? *IEEE Eng Med Biol Mag*. 2004;23:26-27.
21. Liang HD, Blomley MJ. The role of ultrasound in molecular imaging. *Br J Radiol*. 2003;76(suppl2):S140-S150.
22. Lindner JR. Molecular imaging with contrast ultrasound and targeted microbubbles. *J Nucl Cardiol*. 2004;11:215-221. [Abstract](#)
23. Lucignani G, Bombardieri E. Molecular imaging: seeing the invisible beyond the "hot spot." *Q J Nucl Med Mol Imaging*. 2004;48:1-3.
24. Luker GD, Piwnica-Worms D. Molecular imaging in vivo with PET and SPECT. *Acad Radiol*. 2001;8:4-14. [Abstract](#)
25. Luker GD. Special conference of the American Association for Cancer Research on Molecular Imaging in Cancer: linking biology, function, and clinical applications in vivo. *Cancer Res*. 2002;62:2195-2198. [Abstract](#)
26. Massoud TF, Gambhir SS. Molecular imaging in living subjects: seeing fundamental biological processes in a new light. *Genes Dev*. 2003;17:545-580. [Abstract](#)
27. McCaffrey A, Kay MA, Contag CH. Advancing molecular therapies through in vivo bioluminescent imaging. *Mol Imaging*. 2003;2:75-86. [Abstract](#)
28. Meade T. Seeing is believing. *Acad Radiol*. 2001;8:1-3. [Abstract](#)
29. Nichol C, Kim EE. Molecular imaging and gene therapy. *J Nucl Med*. 2001;42:1368-1374. [Abstract](#)
30. Nichol C, Kim EE. Molecular imaging and gene therapy. *J Nucl Med*. 2001;42:1368-1374. [Abstract](#)
31. Phelps ME. Inaugural article: positron emission tomography provides molecular imaging of biological processes. *Proc Natl Acad Sci U S A*. 2000;97:9226-9233. [Abstract](#)
32. Phelps ME. PET: the merging of biology and imaging into molecular imaging. *J Nucl Med*. 2000;41:661-681. [Abstract](#)
33. Pomper MG, Hammoud DA. Positron emission tomography in molecular imaging. Could the promise of personalized patient care be reaching fruition? *IEEE Eng Med Biol Mag*. 2004;23:28-37.
34. Pomper MG. Molecular imaging: an overview. *Acad Radiol*. 2001;8:1141-1153. [Abstract](#)
35. Price P. PET as a potential tool for imaging molecular mechanisms of oncology in man. *Trends Mol Med*. 2001;7:442-446. [Abstract](#)
36. Ritman EL. Molecular imaging in small animals -- roles for micro-CT. *J Cell Biochem Suppl*. 2002;39:116-124. [Abstract](#)
37. Rowland DJ, Lewis JS, Welch MJ. Molecular imaging: the application of small animal positron emission tomography. *J Cell Biochem Suppl*. 2002;39:110-115. [Abstract](#)
38. Rudin M, Weissleder R. Molecular imaging in drug discovery and development. *Nat Rev Drug Discov*. 2003;2:123-131. [Abstract](#)
39. Ryan A, Scarble H. Visualization of the dynamics of gene expression in the living mouse. *Mol Imaging*. 2004;3:33-42. [Abstract](#)
40. Seddon BM, Workman P. The role of functional and molecular imaging in cancer drug discovery and development. *Br J Radiol*. 2003;76(suppl2):S128-S138.
41. Strauss HW, Grewal RK, Pandit-Taskar N. Molecular imaging in nuclear cardiology. *Semin Nucl Med*. 2004;34:47-55. [Abstract](#)
42. Sullivan DC, Ferrari M. Nanotechnology and tumor imaging: seizing an opportunity. *Mol Imaging*. 2004;3:364-369. [Abstract](#)
43. Thomasson DM, Gharib A, Li KC. A primer on molecular biology for imagers VIII. Equipment for imaging molecular processes. *Acad Radiol*. 2004;11(suppl):85-96.
44. Thrall JH. Molecular imaging and molecular biology. *Acad Radiol*. 2003;10:1213-1214. [Abstract](#)
45. Weissleder R. Molecular imaging: exploring the next frontier. *Radiology*. 1999;212:609-614. [Abstract](#)
46. Weissleder R, Mahmood U. Molecular imaging. *Radiology*. 2001;219:316-333. [Abstract](#)
47. Weissleder R. Scaling down imaging: molecular mapping of cancer in mice. *Nat Rev Cancer*. 2002;2:11-18. [Abstract](#)
48. Wickline SA, Lanza GM. Molecular imaging, targeted therapeutics, and nanoscience. *J Cell Biochem Suppl*.

- 2002;39:90-97. [Abstract](#)
49. Gambhir SS. The Henry Wagner Plenary Session: molecular imaging -- the next generation of imaging strategies. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada.
 50. VanBrocklin H (organizer). Categorical seminar: molecular imaging 101. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada.
 51. Penuelas I, Boan JF, Mazzolini GD, et al. Kinetics of [f-18]-FHBG accumulation in HSV1-tk transduced tumors: a pilot study in hepatocarcinoma cancer patients. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 102.
 52. Kuruppu D, Yu M, Wang X, Zu A, Brownell AL, Tanabe K. Imaging viral replication during viral oncolysis of tumors by microPET imaging. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 104.
 53. Alauddin M, Shahinian A, Conti PS. Evaluation of 2'-deoxy-2'-fluoro-5-substituted-1-b-D-arabinofuranosyluracils as markers for suicide gene expression in breast cancer cells. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 103.
 54. Rajendran JG, Koh W, Peterson LM, et al. [F-18]FMISO PET hypoxia imaging in cervical cancer: preliminary results of a novel and noninvasive method characterizing and quantifying hypoxia. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 123.
 55. Pugachev A, Carlin S, Burgman P, et al. A tumor model for non-invasive imaging of hypoxia-induced gene expression: validation and demonstration of utility. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 129.
 56. Souvatzoglou M, Roeser B, Grosu A, et al. Tumor hypoxia imaging with 18F-FAZA in head and neck cancer. A pilot study. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 124.
 57. Beck R, Lebschi JA, Huisman MC, et al. Predictive value of 18F-FAZA uptake for success of radiotherapy, hypoxia directed chemotherapy (tirapazamine) and combined radiochemotherapy. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 125.
 58. Beck R, Picchio M, Haubner R, et al. Intratumoral distribution and correlation of 18F-FAZA, 125I-gluco-RGD and HIF-1 α expression in a murine tumor hypoxia model. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 126.
 59. Strauss LG, Dimitrakopoulou-Strauss D, Koczan D, Pan L, Hoffend J, Haberkorn U. Early effects of Folfex treatment on tumor metabolism and gene expression. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 449.
 60. Strauss LG, Dimitrakopoulou-Strauss A, Klippel S, et al. Colorectal carcinoma: searching for new diagnostic targets using gene chip data. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 579.
 61. Jadvar H, Li X, Shahinian A, Park R, Tohme M, Conti P. Longitudinal microPET studies of tumor growth pattern and glucose metabolism in human prostate cancer murine xenografts. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 1251.

Refining Pediatric Cancer Management Through PET and PET-CT

Hossein Jadvar, MD, PhD

[F-18]-fluorodeoxyglucose (FDG) positron emission tomography (PET) is recognized as a powerful imaging technique for a variety of disease conditions, mainly cancer, in adults. FDG PET is also emerging as an important tool in evaluating children with a number of disease states. Although childhood cancer can be considered relatively rare, cancer is second only to trauma as a cause of death in children. There is marked variation in the incidence rates of specific cancers at different ages in children. It is important to consider the potential causes of misinterpretation of FDG PET that relate to physiologic FDG distribution in children. High FDG uptake is typically seen in the thymus, in skeletal growth centers, and in brown adipose tissue. Elevated bone marrow FDG uptake has been observed in patients as many as 4 weeks following completion of treatment with granulocyte colony-stimulating factor.^[1-18]

The emergence of PET applications in pediatric oncology was highlighted at the Society of Nuclear Medicine meeting, on June 18-22, 2005 in Toronto, Ontario, Canada, in a host of scientific sessions dedicated to this important topic. Two studies reported on the utility of intravenous contrast enhancement and the dosimetry of computed tomography (CT) in pediatric PET-CT applications. Colleagues, from the Harvard Children's Hospital in Boston, Massachusetts, and University of California at Davis, demonstrated that very low dose CT (80 kilovolt [peak] [kV{p}], 10 mA, .5 second per rotation at 1.5:1 pitch) provided adequate CT-based attenuation correction.^[19] Klein and coworkers^[20] showed that although contrast-enhanced CT increased the accuracy of PET-CT at diagnosis of lymphoma, non-enhanced CT was adequate for follow-up studies.

PET-CT Fusion Studies Superior to Either PET or CT Alone

Several studies concentrated on the clinical applications. Strauss and colleagues,^[21] from Munich, Germany, compared the combined analysis of CT and PET with each imaging modality alone in pediatric Hodgkin's lymphoma. The CT scans were performed at a mean interval of 8 days from the PET studies. Histology or follow-up of at least 6 months was employed as the standard of reference for imaging findings. The sensitivity and specificity of PET alone, CT alone, and combined PET and CT image analysis were 91%, 89%, and 95%, and 88%, 36%, and 83%, respectively. The study authors conclude that combined PET and CT image analysis is more accurate than either image modality alone. In a related study, Rekhman and coworkers,^[22] from New York, evaluated the role of serial whole-body FDG PET in the evaluation of treatment and detection of relapse in 17 children with Hodgkin's lymphoma and reported a sensitivity of 100% and a specificity of 75%. Another study from the group at the University of Pennsylvania, Philadelphia, Pennsylvania, showed that FDG PET is a useful imaging tool in the initial evaluation and follow-up of pediatric lymphoma patients and superior to conventional imaging for assessment of early response to therapy.^[23] The same investigators also reported on the use of FDG PET and magnetic resonance (MR) spectroscopy as predictors of local recurrence in pediatric brain tumors.^[24,25] FDG PET was found to show good agreement with MR spectroscopy for detecting high-grade recurrent brain tumors.^[24] For detecting brain tumor recurrence, PET had a sensitivity, specificity, negative predictive value, and positive predictive value of 96%, 60%, 86%, and 73%, respectively.^[25]

In another study by Loeffler and colleagues,^[26] from Muenster, Germany, the diagnostic utility of FDG PET in children with chronic inflammatory bowel disease was assessed. When compared with endoscopy as the standard of reference, the sensitivity and specificity were 87% and 66% for PET, 56% and 81% for abdominal ultrasound, and 37% and 100% for enteroclysis. When compared with histology as the standard of reference, the sensitivity and specificity were 90% and 65% for PET, 56% and 92% for abdominal ultrasound, and 33% and 94% for enteroclysis. The investigators concluded that FDG PET offers an accurate, noninvasive diagnostic imaging method for localizing and depicting the acuity of inflammation in children with inflammatory bowel disease. Gelfand and associates,^[27] from the Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, also reported on the frequency of equivocal studies in pediatric FDG PET body imaging patients who had received premedication (fentanyl or diazepam) to block FDG uptake in brown fat. The study concluded that with premedication, equivocal findings on PET were relatively infrequent when correlated with CT. These same investigators have also published their results.^[28] Recent studies, however, have reported that simple ambient temperature control may offer an efficient and effective method for minimizing brown fat FDG uptake.^[29,30]

FDG PET has been shown to be useful in the imaging evaluation of many pediatric tumors. The expansion of PET and PET-CT imaging systems to children's hospitals will facilitate the multi-institutional trials that are necessary to define the precise roles of this powerful imaging technology in pediatrics. It is expected that the future data will show that FDG PET does contribute unique, valuable information for the care of childhood tumors.

References

1. Borgwardt L, Larsen HJ, Pedersen K, Hojgaard L. Practical use and implementation of PET in children in a hospital PET Center. *Eur J Nucl Med Mol Imaging*. 2003;30:1389-1397. [Abstract](#)
2. Hawkins DS, Rajendran JG, Conrad EU III, et al. Evaluation of chemotherapy response in pediatric bone sarcomas by [F-18]-fluorodeoxy-D-glucose positron emission tomography. *Cancer*. 2002;97:3277-3284.
3. Hudson MM, Krasin MJ, Kaste SC. PET imaging in pediatric Hodgkin's lymphoma. *Pediatr Radiol*. 2004;34:190-198. [Abstract](#)
4. Jadvar H, Connolly LP, Shulkin BL, et al. Positron emission tomography in pediatrics. In: LM Freeman, ed. *Nuclear Medicine Annual*. Philadelphia, Pa: Lippincott Williams & Wilkins; 2000:53-83.
5. Jadvar H, Connolly LP, Shulkin BL. Pediatrics. In: Wahl RL, ed. *Principles and Practice of Positron Emission Tomography*. Philadelphia, Pa: Lippincott Williams & Wilkins; 2002:395-410.
6. Jadvar H, Connolly LP, Shulkin BL. PET imaging in pediatric disorders. In: Valk PE, Bailey DL, Townsend DW,

- Maisey MN, eds. Positron Emission Tomography: Basic Science and Clinical Practice. London, United Kingdom: Springer-Verlag; 2003:755-774.
7. Jadvar H, Alavi A, Mavi A, Shulkin BL. PET in pediatric diseases. In: Alavi A, ed. Radiologic Clinics of North America. Vol. 43. Philadelphia, Pa: Elsevier Saunders, Inc.; 2005:135-152.
 8. Kaste SC. Issues specific to implementing PET-CT for pediatric oncology: what we have learned along the way. *Pediatr Radiol.* 2004;34:205-213. [Abstract](#)
 9. Krasin MJ, Hudson MM, Kaste SC. Positron emission tomography in pediatric radiation oncology: integration in the treatment-planning process. *Pediatr Radiol.* 2004;34:214-221. [Abstract](#)
 10. O'Hara SM, Donnelly LF, Coleman RE. Pediatric body applications of FDG PET. *AJR Am J Roentgenol.* 1999;172:1019-1024. [Abstract](#)
 11. Patel PM, Alibazoglu H, Ali A, Fordham E, LaMonica G. Normal thymic uptake of FDG on PET imaging. *Clin Nucl Med.* 1996;21:772-775. [Abstract](#)
 12. Roberts EG, Shulkin BL. Technical issues in performing PET studies in pediatric patients. *J Nucl Med Technol.* 2004;32:5-9. [Abstract](#)
 13. Ruotsalainen U, Suhonen-Povli H, Eronen E, et al. Estimated radiation dose to the newborn in FDG-PET studies. *J Nucl Med.* 1996;37:387-393. [Abstract](#)
 14. Shulkin BL, Chang E, Strouse PJ, et al. PET FDG studies of Wilms tumors. *J Pediatr Hematol Oncol.* 1997;19:334-338. [Abstract](#)
 15. Shulkin BL, Mitchell DS, Ungar DR, et al. Neoplasms in a pediatric population: 2-[F-18]-fluoro-2-deoxy-D-glucose PET studies. *Radiology.* 1995;194:495-500. [Abstract](#)
 16. Shulkin BL. PET applications in pediatrics. *Q J Nucl Med.* 1997;41:281-291. [Abstract](#)
 17. Shulkin BL. PET imaging in pediatric oncology. *Pediatr Radiol.* 2004;34:199-204. [Abstract](#)
 18. Weinblatt ME, Zanzi I, Belakhlef A, et al. False-positive FDG-PET imaging of the thymus of a child with Hodgkin's disease. *J Nucl Med.* 1997;38:888-890. [Abstract](#)
 19. Fahey FH, Palmer MR, Strauss KJ, Zimmerman RE, Badawi RD, Treves ST. Dosimetry and image quality associated with low-dose CT-based attenuation correction for pediatric PET. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 212.
 20. Klein M, Libson E, Chisin R, Weintraub M, Koplewitz B. Contrast-enhanced CT vs non-enhanced low-dose CT in combined PET-CT for pediatric lymphoma. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 215.
 21. Strauss J, Pfluger T, Hahn K. Combined image analysis in pediatric Hodgkin's lymphoma: F18-FDG-PET and computed tomography. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 214.
 22. Rekhman K, Levine JM, Weiner MA, et al. The sensitivity of whole-body positron emission tomography in the diagnosis and follow up of pediatric patients with Hodgkin's disease: a retrospective pilot study. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 219.
 23. Hernandez-Pampaloni M, Takalkar A, Yu JQ, Zhuang H, Alavi A. Role of FDG PET imaging and correlation with CT in staging and early follow-up of pediatric lymphomas. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 221.
 24. Hernandez-Pampaloni M, Takalkar A, Huang S, Yu JQ, Zhuang H, Alavi A. FDG PET and MR spectroscopy as predictors of local recurrence of disease in pediatric brain tumors. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 216.
 25. Hernandez-Pampaloni M, Takalkar A, Huang S, Yu JQ, Zhuang H, Alavi A. Assessment of suspected brain tumor recurrence in children: comparison between 18FDG PET imaging and MRI. FDG PET and MR spectroscopy as predictors of local recurrence of disease in pediatric brain tumors. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 220.
 26. Loeffler M, Weckesser M, Franzius C, Schober O, Zimmer KP. FDG-PET in chronic inflammatory bowel disease in children. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 223.
 27. Gelfand MJ, Vo NJ. FDG-PET body imaging in a pediatric population that has received pre-medication to block FDG uptake in brown adipose tissue: equivocal studies and CT correlation. Program and abstracts of the Society of Nuclear Medicine 52nd Annual Meeting; June 18-22, 2005; Toronto, Ontario, Canada. Abstract 223.
 28. Gelfand MJ, O'hara SM, Curtwright LA, Maclean JR. Pre-medication to block [18F]FDG uptake in the brown adipose tissue of pediatric and adolescent patients. *Pediatr Radiol.* 2005; [Epub ahead of print].
 29. Cohade C, Mourtzikos KA, Wahl RL. "USA-Fat": prevalence is related to ambient outdoor temperature-evaluation with 18F-FDG PET/CT. *J Nucl Med.* 2003;44:1267-1270. [Abstract](#)
 30. Garcia CA, Van Nostrand D, Majd M, et al. Benzodiazepine-resistant "brown fat" pattern in positron emission tomography: two case reports of resolution with temperature control. *Mol Imaging Biol.* 2004;6:368-372. [Abstract](#)

Authors and Disclosures

As an organization accredited by the ACCME, Medscape requires everyone who is in a position to control the content of an education activity to disclose all relevant financial relationships with any commercial interest. The ACCME defines "relevant financial relationships" as "financial relationships in any amount, occurring within the past 12 months, that create a conflict of interest."

Medscape encourages Authors to identify investigational products or off-label uses of products regulated by the U.S. Food and Drug Administration, at first mention and where appropriate in the content.

Author

Hossein Jadvar, MD, PhD

Assistant Professor of Radiology and Biomedical Engineering, Keck School of Medicine, University of Southern California, Los Angeles

Disclosure: Hossein Jadvar, MD, PhD, FACNM, FACNP, has disclosed no relevant financial relationships.

Editor

Robert Chevrier

Program Director/Site Editor, Medscape, Inc.

Disclosure: Robert Chevrier has disclosed no relevant financial relationships.

Registration for CME credit, the post test and the evaluation must be completed online.

To access the activity Post Test and Evaluation link, please go to:

http://www.medscape.com/viewprogram/4437_index