

**Washington State Health Care Authority, HTA Program
Final Key Questions and Background
PET For Lymphoma**

Introduction

HTA has selected positron emission tomography, alone or combined in one system with CT (PET) for Lymphoma to undergo a health technology assessment where an independent vendor will systematically review the evidence available on the safety, efficacy, and cost-effectiveness. HTA posted the topic and gathered public input on all available evidence. HTA published the Draft Key Questions to gather input about the key questions and any additional evidence to be considered in the evidence review, and will review the public comments submitted and finalize the key questions. Key questions guide the development of the draft evidence report.

Despite varying levels of evidence supporting beneficial health outcomes, clinical use of PET in the evaluation, treatment, and monitoring of lymphoma appears to be growing. There are concerns about efficacy, safety, cost, and health impact of use of PET for lymphoma. Information about when PET for lymphoma is clinically indicated and what health outcomes it improves is needed.

At this phase, HTA is requesting public comments on the key questions. Key questions will direct the gathering, review, and summary of the evidence for the report. The HTA considers all public comments and we are particularly interested in comments that include information on whether the key questions will identify available evidence about the technology's safety, efficacy, effectiveness, and cost effectiveness. Once the key questions are finalized, the vendor will search for evidence and compile a draft report. The draft report will then be published for review and public comment.

Key Questions

1. What is the evidence of accuracy of PET (alone or combined on one system with CT) imaging for lymphoma?
 - Describe sensitivity, specificity, and other key test characteristics in screening and initial diagnosis
 - Describe sensitivity, specificity, and other key test characteristics in staging/re-staging and surveillance.
 - Include comparators of MRI, CT, Gallium Scintigraphy, biopsy

2. What is the evidence of clinical effectiveness of PET imaging in patients with known or suspected lymphoma compared to CT and MRI when used as an adjunct to CT or MRI or Gallium Scintigraphy, including:
 - Reduced need for other tests
 - Planning or changing patient management (e.g. continuation of chemotherapy)
 - Improvement in quality of life
 - reductions in morbidity and mortality
 - improved patient outcomes with vs. without PET

3. What is the evidence that PET imaging in patients with known or suspected lymphoma has differential efficacy or safety issues in sub populations? Including consideration of:
 - a. Patient age, gender, characteristics or evidence based patient selection criteria

- b. Type of scanning machine and software, reader training, and other operational factors
 - c. Provider type, setting or other provider characteristics
 - d. Health care system type, including worker's compensation, Medicaid, state employees
4. What is the evidence of PET for lymphoma safety profile?
 - a. Adverse events type and frequency (mortality, major morbidity, other)
 5. What is the evidence about the cost impact of PET for patients with known or suspected lymphoma? Including consideration of:
 - a. Costs in short term
 - b. Costs in long term
 - c. Cost effectiveness

Technology Background

It is estimated that 74,000 US individuals will be diagnosed with lymphoma (about 65,500 non-Hodgkin lymphoma and 8,500 Hodgkin lymphoma). Successful treatment by complete remission of lymphoma, depending on stage, and 5 year survival rates are as high as 80 to 90%. Accurate information about diagnosis and staging is important for planning the most appropriate treatment strategy; as well assessing how a person is responding to treatment, and monitoring if the cancer has recurred. Physical symptoms; palpation; biopsy; MRI; CT; PET and PET/CT can used to assess patients. Positron emission tomography and PET/CT (collectively PET), are increasingly performed to inform restaging (assessment of treatment response), as well as diagnosis, staging, and monitoring of recurrence of cancer.

Technology:

PET produces a three-dimensional image of certain changes (biochemical processes) in the body by tracking where radioactive molecules (most commonly fluorodeoxyglucose or FDG) accumulate, which can indicate presence and extent of abnormal function associated with tumor tissue. PET/CT combines PET and a computed tomography in a single system so that images acquired from both devices can be taken sequentially in the same session and combined. The potential advantage of the functional imaging obtained by PET can be correlated with anatomical imaging obtained from CT.

PET has diffused rapidly, following several studies showed that PET or PET/CT used in Hodgkin lymphoma and an aggressive non-Hodgkin lymphoma at the end of front-line, salvage, or high-dose therapy provided accurate information about remaining cancer. It has since diffused to use in other lymphoma types and many stages of lymphoma diagnosis, treatment, and monitoring; guidelines for use are primarily based on expert consensus; and information about the evidence of timing of PET/CT; need for repeated scans and effect, compared to other assessment means, on use of invasive tests, therapeutic choices, and health outcomes is needed.

Dr. Eary is Professor of Radiology , working in Nuclear Medicine and Molecular Imaging. Her background includes specialty board certifications in Nuclear Medicine, Laboratory Medicine and Pathology.

Throughout her career, she has had a focus on cancer imaging and therapy (including lymphoma and metastatic disease). During her tenure as chief of Nuclear Medicine for the University of Washington Hospital,s she instituted the clinical PET service, one of the earliest of its type in the US. Currently, her research involves cancer imaging and translational research with new radiopharmaceuticals for PET and clinical trials. She is also engaged in clinical practice, and lecturing.

Participant Conflict of Interest Guideline

Introduction

The HTCC Workgroup is a public service workgroup established to safeguard the public interest by identifying medical tests and treatments where evidence shows they are safe, effective, and cost-effective. Balance, independence, objectivity and scientific rigor are a basis for public trust and crucial to the credibility and integrity of decisions.

Guiding Principle

Conflict of Interest decisions must be disclosed and balanced to ensure the integrity of decisions while acknowledging the reality that interests, and sometimes even conflicting interests, do exist. Individuals that stand to gain or lose financially or professionally, or have a strong intellectual bias need to disclose such conflicts.

For example, the fact that a member or stakeholder is a health care provider that may use a service under review creates a potential conflict. However, clinical and practical knowledge about a service is also useful, and may be needed in the decision making.

Procedure

Declaration of real or potential conflicts of interest, professional, intellectual, or financial is required prior to membership or provision of written or verbal commentary. Participants must sign a conflict of interest form; stakeholders providing comment must disclose conflicts.

The HTCC Chair or HCA Administrator shall make a decision, in his/her sole discretion, as to whether a conflict of interest rises to the level that participation by the conflicted participant could result in a loss of public trust or would significantly damage the integrity of the decision.

HCA defines conflict of interest as any situation in which a voting member or anyone who provides written or verbal testimony regarding products, services, or technologies discussed or voted on during the workgroup meeting, has a relationship with a manufacturer of any commercial products and / or provider of services discussed or voted on during the meeting. Relationship extends to include immediate family member(s) and / or any entity in which the member or person testifying may have an interest.

A relationship is considered as:

1. Receipt or potential receipt of anything of monetary value, including but not limited to, salary or other payments for services such as consulting fees or honoraria in excess of \$10,000.
2. Equity interests such as stocks, stock options or other ownership interests in excess of \$10,000 or 5% ownership, excluding mutual funds and blinded trusts.
3. Status of position as an officer, board member, trustee, owner or employee of a company or organization representing a company, association or interest group.
4. Loan or debt interest; or intellectual property rights such as patents, copyrights and royalties from such rights.
5. Manufacturer or industry support of research in which you are participating.
6. Any other relationship that could reasonably be considered a financial, intellectual, or professional conflict of interest.
7. Representation: if representing a person or organization, include the organization's name, purpose, and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).
8. Travel: if an organization or company has financially paid your travel accommodations (e.g. airfare, hotel, meals, private vehicle mileage, etc).

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of \$10,000		X
2.	Equity interests such as stocks, stock options or other ownership interests		X
3.	Status of position as an officer, board member, trustee, owner		X
4.	Loan or intellectual property rights		X
5.	Research funding		X
6.	Any other relationship		X

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		X

7. If yes, Provide Name and Funding Sources: _____

	Potential Conflict Type	Yes	No
8.	Travel: if an organization or company has financially paid your travel accommodations (e.g. airfare, hotel, meals, private vehicle mileage, etc).		X

8. If yes, Provide Name of Organization / Company and Disclose Travel Accommodations:



If you believe that you do not have a conflict but are concerned that it may appear that you do, you may **attach additional sheets** explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X

[Handwritten Signature]

Signature

7/14/11

Date

J. F. EARLY, M.D.

Print Name

FOR QUESTIONS:

Denise Santoyo, Health Care Authority, 360-923-2742,
PO Box 42712, Olympia, WA 98504-2712

First Name: <u>JANET</u>		Last Name: <u>EARLY</u>	
Organization: <u>UNIVERSITY OF WASHINGTON</u>			
Employee	<input checked="" type="radio"/> Yes	<input type="radio"/> No	Contractor: <input type="radio"/> Yes <input checked="" type="radio"/> No
Please review the Conflict of Interest Policy and Definitions prior to completing this form.			
Business Relationships:		Place an X in the appropriate box.	
		Yes	No
1.	Based on the above definitions, do you or your company or members of your family have or expect to have in the next 12 months:		<input checked="" type="checkbox"/>
	A. a significant financial interest in a financially interested business?		
		If you answered "yes", please answer each question below:	
		I. Describe the nature of your (and/or your family members') or your company's financial interest and your relationship with the business and list the business(es). If you are a consultant or hold a position in the company, please also describe the specific services you provide to the company in that role.	
		II. Indicate the projects that are sponsored by the business that involve technology owned or licensed by the business, or are otherwise associated with the business:	
		III. Describe any controls already in place that may mitigate any potential conflict of interest (e.g., outside data analysis, data safety monitoring, blinded trial):	

**OHSU Center for Evidence-based Policy
Conflict of Interest Disclosure Form**

This form must be completed by all employees of the Center on an annual basis, and by all consultants, contractors and outside vendors prior to beginning work on any Center projects. A revised Conflict of Interest form is required prior to the annual update if any response to an item has changed from "NO" to "YES".

		Place an X in the appropriate box.	
		Yes	No
	B. a significant financial interest in an outside business contributing funds to the OHSU Foundation which are under your control and of direct benefit to your research activities?	<input checked="" type="checkbox"/>	<input type="checkbox"/>
		If you answered "yes", please answer the question below:	
		Describe your (and/or your family members'), or your company's relationship with the business and list the business(es). Describe the purpose of the funds and explain which research activities are affected:	

Intellectual Property:		Place an X in the appropriate box.		Yes	No
1.	Are you or your company the inventor(s) of a licensed or copyrighted product or technology, or a technology assigned to an outside business that you continue to utilize in any of your current or pending research projects?	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
		If you answered "yes", please answer the questions below:			
		List the invention(s) and the business(es) that have been assigned or that have been licensed the technology.			
		Indicate which projects utilize the technology(s) and/or are sponsored by the business(es) that licensed the technology.			
2.	In the previous 12 months, did you or your company create, discover, or reduce to practice an invention to which title has not been assigned to OHSU?	<input type="checkbox"/>	<input type="checkbox"/>		
		List the invention(s). To whom is title assigned? Was this invention prior to your employment at OHSU?			

Student Involvement:		Place an X in the appropriate box.		Yes	No
1.	In the previous 12 months, did you involve any of your students in OHSU projects that are sponsored by a business in which you or a family member has a significant financial interest?				X
2.	In the previous 12 months, did you involve any of your students in remunerated participation in professional activities for an outside business in which you or a family member has a significant financial interest?				X
		<i>If you answered "yes" to either of questions above, please complete the following information:</i>			
		List the project(s), student(s) involved, and the business(es). Describe the activities/involvement of students. Describe your (your family member's) relationship with the business.			

Previous Disclosure Information:		Place an X in the appropriate box.		Yes	No
1.	<i>Based on your last annual disclosure, did the Conflict of Interest in Research committee require a management plan?</i>				
		<i>If you answered "yes", please complete the following information:</i>			
	Have there been any publications or presentations resulting from your research related to your financial interests since your last management plan was issued? (check appropriate box)				X
		<i>If yes, please provide any references or presentations where a statement of your financial interests was included. If the public disclosure statement was not included please explain why.</i>			

Contractor:

Signature/Title

[Handwritten Signature]

Date

7/14/11

CURRICULUM VITAE

Janet F. Eary, M.D.

ADDRESS

University of Washington Medical Center
Division of Nuclear Medicine
Box 356113
1959 N.E. Pacific
Seattle, WA 98195-6113
(206) 548-4240
(206) 548-4496 FAX

DATE OF BIRTH

November 10, 1954
Grand Rapids, Michigan

EDUCATION

University of Michigan, B.S. (honors), 1976.
Michigan State University, E. Lansing, M.D., 1980.

POST GRADUATE TRAINING

Residency, Pathology, University of Washington, 1980 - 1983.

Residency, Nuclear Medicine, University of Washington, 1983 - 1985.

Fellow, Nuclear Medicine, University of Washington, 1985 - 1986.

OTHER PROFESSIONAL EXPERIENCE

Michigan Primary Care Preceptorship, Burns Clinic,
Petoskey, Michigan 1978.

Michigan Heart Association Grant, Development of an assay for platelet
adhesion to collagen in vitro for evaluation of von Willibrand's disease.
University of Michigan Medical Center, 1979.

ACADEMIC APPOINTMENTS

Professor, Department of Radiology, Director, Division of Nuclear Medicine,
University of Washington, Chief, University of Washington Medical Center
Clinical Nuclear Medicine Services, 6/96 – 11/04.

Director of Research, Department of Orthopedics, Childrens Hospital and Medical Center, 2007- present

Professor, Department of Orthopedics 2005- present

Director, University of Washington Molecular Imaging Center.
1/2003 – present.

Adjunct Professor, Department of Pathology, University of Washington,
6/1996 - present.

Affiliate Investigator, Division of Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, Washington, 7/97 - present.

Associate Professor, Department of Radiology, Division of Nuclear Medicine, University of Washington, 6/1991 - 1996.

Adjunct Associate Professor, Department of Pathology, University of Washington, 6/1991 - present.

Assistant Professor, Department of Radiology, Division of Nuclear Medicine, University of Washington, 1987 - 6/1991.

Adjunct Assistant Professor, Department of Pathology, University of Washington, 1987 - present.

Pathology Attending Staff, Autopsy Service. University of Washington Medical School, 1985 - 1994.

Instructor, Department of Radiology, Division of Nuclear Medicine, University of Washington, 1986 - 1987.

Teaching fellow, Fundamentals of Patient Care. Michigan State University, College of Human Medicine, 1979.

Teaching fellow, Applied Anatomy and Basic Patient Interviewing Skills, Michigan State University, College of Human Medicine, 1978.

Teaching fellow, Histology course, Michigan State University, College of Human Medicine, 1977.

HOSPITAL APPOINTMENTS

University of Washington Medical Staff Administrative Committee,
July 2001 – present.

Acting Chief, Mammography Section. April 2001- July 2002.

Seattle Cancer Care Alliance Staff, January 2001 – present.

Fred Hutchinson Cancer Research Center Clinical Staff, 1996 – present.

Associate Medical Staff, Harborview Medical Center, January 1992 - present.

Associate Medical Staff, Department of Veterans Affairs Medical Center,
Seattle, July 1992 - present.

University of Washington Medical Center Staff, 1980 – present.

HONORS

Distinguished Scientist Award, Western Regional Chapter of the Society of Nuclear Medicine. October 2001.

Phillip M. Johnson Lecture, Columbia College of Physicians and Surgeons,
New York City, New York. 2001.

New Investigators - Science in Medicine Lectureship, University of Washington, October, 1989.

Regents Alumni Scholar, University of Michigan, 1972 - 1973.

Undergraduate Honors in Botany, Thesis title "Photosynthesis: Localization of cytochrome b 559 in photosystem II by cyanide inhibition".

OTHER ACADEMIC ACTIVITIES

Nuclear Medicine Residency Training Program Director 1996- 2005

Biomedical Research Integrity Series, Seminar Leader, "Use of Animals in Laboratory Research." August 1-2, 2001.

Masters thesis advisor: Deborah McBaugh, "Radiation Safety aspects of Radioimmunotherapy". Dept. Health physics, 1988-1989.

Ph.D. Thesis Committee: Ken Pollard, Dept. of Bioengineering

Lecturer: UW Conjoint 100 course in Health Science for undergraduates. 1989.

Medical Student Thesis advisor: Mark Diebert, 1989.

Medical Student Thesis advisor: Andrew Howlett, 1995 - 1996 academic year.

Medical Student Thesis advisor: Sarah Rice, 1997. Sponsor for American Cancer Society Medical Student Fellowship. Ms. Rice received the grade of “excellent”.

Undergraduate Student Thesis advisor: Kathryn Shields, 1999.
Massachusetts Institute of Technology Nuclear Engineering Program.

Visiting Scientist Sponsor for PET Project in Bone metabolism Imaging. Dr. Winfried Brenner, M.D., Kiel Germany 2002-2003.

Masters Thesis Committee Extern Reviewer: Katheryn McKeown. “ Spatial Heterogeneity in FDG PET Tumor Volumes, Boundary Shape Adapted Contour Analysis. Department of Statistics, University College, Cork, Ireland. 2005-2007.

PhD Thesis Extern Reviewer: Jacqueline Kirrane University College Cork 12/2008

Molecular Medicine/Pathology Conjoint 514: UW course Molecular Medicine Seminar (3 credit hours) Course chair 2008-2010

UW Biomedical Research Integrity Program Discussion leader –August 2010

CERTIFICATION AND LICENSURE

American Board of Pathology
Anatomic Pathology - Certification, 1984
Clinical Pathology - Certification, 1985
American Board of Nuclear Medicine Certification, 1986, voluntary re-certification 2009.

Medical Licensure: Washington, 1980

SOCIETIES

Society of Nuclear Medicine Pacific Northwest Chapter Membership
Chairman, 1988-1989.

Society of Nuclear Medicine
National Board of Trustees, 1993-1998.
Therapy Council Vice President, 2001 – 2002.

World Federation of Nuclear Medicine and Biology Therapy Council.

Association of University Radiologists

University of Washington Housestaff Association Vice President, 1980 - 1981

Radiological Society of North America, Active Member September 1998 - present.

European Society of Nuclear Medicine 1996-present

Connective Tissue Oncology Society 2006-present

Children's Oncology Group 2006-present

American Association of Cancer Researchers 2006-present

American Association of Orthopedic Surgeons 2006-present

EDITORIAL RESPONSIBILITIES

Editorial Board: Journal of Nuclear Medicine 2006-present

Editorial Consultant: *Lancet*, March-2005 - present

Editorial Board: *Nuclear Medicine Communications*, 1991 - present.

Editorial Board: *Oncology Reports*, 1998 - present.

NATIONAL/REGIONAL ACTIVITIES

NCI Translational Research Working Group January 2006-present

Children's Oncology Group (COG) Bone tumors Steering Committee, June 2006-present

REVIEWS

National Institutes of Health Cancer Center Support Grant Program site visitor, University of Iowa. September 14-16, 2010.

National Institutes of Health Special Review Section, Quantitative Imaging U01 grants, Chair, March 4, 2010.

National Institutes of Health Biomedical Scientist Loan Repayment Program reviewer, May 2010

National Institutes of Health Cancer Center Support Grant Program site visitor, University of Utah. October, 2009.

National Institutes of Health Study Section regular member Clinical Molecular Imaging Probes (CMIP). 2009- present.

National Institutes of Health Cancer Center Support Grants program site visit reviewer, University of Chicago. October 29-31, 2007.

National Institutes of Health Study Section on Imaging Quick Trials, 2007 Review Committee chair 2009-present

National Institutes of Health Study section on Vaccines and Infectious Diseases, ad hoc reviewer. 2006-2007

NIH Multidisciplinary Clinical Research Career Development Program June 2005- present

National Institutes of Health, Radiology, Nuclear Medicine Study Section Member, (MEDI) 2002 – 2007. ad hoc member, 2008, 2009

NCI sponsored Progress Review Group in Sarcoma , member, Imaging Group Leader, July 2003-present

Department of Energy, Grant Review Section Chairman, Cellular Targeted Therapies, May 2001.

NIH Radiology Clinical Center, Radiation Oncology Program Review, May 2001.

Netherlands Institute of Health, PET Clinical Study Review, March 2001.

NIH Radiology Clinical Center, Radiation Oncology Program Review, May 1999.

NIH Radiology Clinical Center, Radiology Program Review, December 9-11, 1999.

NIH Radiology/Nuclear Medicine Study Section Ad Hoc Member. February 24-25, 1998.

NCI/NIH Member of Special Emphasis Panel to review application of a General Clinical Research Center. October 30, 1997.

NCI/NIH Member of Imaging in Treatment Planning Workshop. September 25-26, 1997.

NIH Site Reviewer, Intramural Programs in Radiation Oncology and Radiology, May 28-29, 1997.

NCI/NIH Special Study Section member for review of linked ROIs for cancer therapy. April 26-28, 1994.

Program Project site visitor: Gyn-Oncology Therapy. November 19-21, 1993.

Special Study Section member for review of linked ROIs for cancer therapy. April 29 - May 1, 1993.

Program Project Site visitor for a malignant brain tumors proposal. Feb. 18-19, 1993.

Immunology/Ob Gyn. Radioimmunotherapy site visit program project. July 21-22, 1992.

NCI/NIH Special Study Section Member for Special Program Projects in Breast Cancer Therapy. May 1992.

Immunology/Ob Gyn site visitor. March 21-22, 1990.

National Institutes of Health Special Study Section Site Visitor, March 8-9, 1990.

ORGANIZATIONS

Pacific Northwest Society of Nuclear Medicine Annual Meeting Program Chairman, Portland Oregon, 2006

Zevalin National Advisory Board, July 2001 – present.

ACRIN PET Imaging Review Committee, 1999-present.

Quadramet National Advisory Board, 3/2000 – present.

Society of Nuclear Medicine Committee on Radiobiological Effects of Ionizing Radiation, 1997 - 2000.

NIH/NCI special working group on Imaging in Radiation Planning, September 1997.

NIH/NCI New Imaging Modalities working group, 1997.

Ohio Cancer Research Associates Grant Reviewer, 1995 - present.

National Council on Radiation Protection and Measurements. Committee 91-1, 1995.

Western Regional Society of Nuclear Medicine Meeting Scientific Program Chairman. Vancouver, Canada, 1993.

Western Regional Society of Nuclear Medicine Annual Meeting. Scientific Program Committee. 1988 - 1993.

American Medical Association Diagnostic and Therapeutic Technology Assessment Panel, 1990 - 1991.

Pacific Northwest Society of Nuclear Medicine Scientific Program Chairman. 1990 - 1991.

Society of Nuclear Medicine Annual Meeting Immunology/Antibody Division Program Sub-Chairman, 1990.

Food and Drug Administration Orphan Drug Section Grant Reviewer. 1990.

United States Pharmacopeia, Committee of Revision, Expert Advisory Panel on Radiopharmaceuticals, 1990 - 2000.

Veterans Administration Eastern Division Merit Grant Review. 1989.

Department of Energy Grant Review. 1988 - present.

Western Regional Society of Nuclear Medicine Mid-winter Meeting. Scientific Program Committee. 1987, 1989.

UNIVERSITY COMMITTEES

Fred Hutchinson Cancer Research center/University of Washington Cancer Consortium Pilot grants review 2005-2007

Fred Hutchinson Cancer Research Center/ University of Washington Cancer Center Consortium Scientific Steering Committee 2002-present

Seattle Cancer Care Alliance Radiation Safety Committee Chairman. 2001 – 2003.

Breast Imaging Advisory Committee. July 2001 – 2002.

UWMC Second Floor Planning Committee, April 2001 – 2002.

University of Washington Medical Center/Fred Hutchinson Cancer Research Center SPORE Advisory Committee. January 2001 – present.

Scientific Affairs Faculty Council, 1994 - 1998.

FDA Sponsored Radioactive Drug Research Committee, 1994 - present.
Chairman, 1994-2004

Radiation Safety Committee, Scientific Executor, 1989 - 2001.

University of Washington "Ride in the Rain" Honorary Co-Chair, 2004, 2005
Winter Bicycle Commuters event

University of Washington School of Medicine working group for the Clinical
Translational Science Program Award

University of Washington Faculty Senate, 2008-2010

Molecular Medicine Executive Committee, 2008-present

University of Washington Clinical Translational Sciences Program (CTSA)
GCRC Protocol Review Committee Chair, 2008- present

Children's Hospital and Medical Center Clinical and Translational
Research Center Steering Committee, 2008- present

RADIOLOGY DEPARTMENT COMMITTEES

Finance Committee, June 2001 – July 2002.

Vice Chair for Operations Search Committee, April 2001 – July 2002.

Radiology Department Finance Committee May 2001-July 2002

Chairman, Mammography Task Force, February –August 2001 July 2002

Clinical Incentive Planning Committee, 2000 – 2001.

Appointments and Promotions Committee, 1999 – 2004.

Imaging Research Laboratory Executive Committee

Larry Mack Endowed Fund Advisory Committee.

FUNDED PROJECTS

Co-Principal Investigator UW PET in Cancer Program Project 2009-present
Project 2 Principal Investigator: Imaging Tumor Proliferation

Project 5 co-Principal Investigator: Factors in Sarcoma Treatment Resistance
Project 5 competing renewal submitted Principal Investigator: Imaging
Multiple Drug Resistance
Project 1 competing renewal submitted co-Investigator: Imaging Tumor
Proliferation

RO1 Principal Investigator, PET in Sarcoma R01 NIH-NCI, 7/95- present

Principle Investigator: Molecular and Radionuclide Therapy Trials Group.
UW site. Society of Nuclear Medicine. May 2005-present

Principle Investigator: Pilot study: Sentinel Node Imaging in synovial cell
and epitheloid sarcomas. 2005-present

Co-Investigator: Multicenter Trial of M-TOR inhibitors in refractory soft
tissue sarcoma. Ariad Pharmaceuticals. June 2005.

Co-Principle Investigator, Imaging Program, ‘A Phase III randomized study
of Imantinib, with or without Bevacizumab in patients with metastatic or
unresectable gastrointestinal stromal tumors.: Intergroup Coalition against
sarcomas members, Southwest Oncology Group membersm and CCOP
Affiliate Medical oncologists, National Trial, sponsored by NCI CTEP,
Medicare, CMS and NCI Cancer Imaging Program. 2005-present

Principle Investigator: C-11 Acetate Imaging in Prostate Cancer, Pilot Study.
2005- 2008

Principle Investigator, Imaging Core, Fred Hutchinson Cancer Research
Center Comprehensive Cancer Center. January 2003- 2008

Principle Investigator, Imaging Program, Fred Hutchinson Cancer Research
Center Comprehensive Cancer Center. January 2003- present

Principle Investigator, NCI Molecular Imaging Network, UW site, November
2003-present

Principle Investigator, Imaging treatment Response in patient with Non-
Hodgkin’s Lymphoma , IDEC Corp, June 2004- present

Co-investigator, F-18 Fluoroestradiol in Prostate Cancer characterization.
NIH/NCI pilot project 1/05-present

Investigator, HER2 Specific T-Cell Infusion Following HER2-Negative
Based Vaccination for Treatment of HER2 Non-expressing malignancy. NIH,
NCI R01, Nora Disis, PI. February 2001 – present.

Co-Principal Investigator, Ho-166 DOTMP in High Dose Treatment of Children with Refractory Ewing's Carcinoma. Seattle Children's Hospital and Medical Center, 2000-present.

Principal Investigator, Ho-166 DOTMP in the High Dose Treatment of Multiple myeloma with Stem Cell Support. Nero Corporation, 1999 – 2002.

Co-Principal Investigator, B₁ Trial for Low Dose I-131 Antibody Treatment of Lymphoma. Coulter Pharmaceuticals, 7/96 - 2002.

Principal Investigator, Biodistribution and metabolism of soluble tumor necrosis factor receptor. Immunex Corp. 11/95 - 1/97.

Co-Principal Investigator, Sm-153 EDTMP in Treatment of Stage D₂ Prostate Cancer with Total Androgen Blockade. 11/95 – 11/98.

PET Program Project in Cancer. NIH-NCI. Principal Investigator, Project 2: Thymidine Imaging in Cancer. 5/95 - present.

PET Program Project in Cancer, NIH-NCI Co-Principle Investigator, Project 5: Imaging Treatment Resistance Mechanisms in Sarcoma. 5/04-present

Principal Investigator, Project IV: Determination of Estrogen Content in Breast Cancer by PET. 5/92 - 4/94.

Antibody Program Project: Therapy of Lymphoma and Leukemia with Radiolabeled Monoclonal Antibodies. NIH-NCI. 6/88-6/00. Principal Investigator, Project III.

Principal Investigator, Nuclear Medicine Core. 6/88 – 2001.

Co-investigator, Nuclear Medicine Core 6/01-2004

Co-Principal Investigator, Sm-153 EDTMP in the Treatment of Hormonal Refractory Prostate Cancer. Phase I/II Trial. Merrell Dow Pharmaceutical Co., 1988 - 1994.

Principal Investigator, Quantitation of Radiolabeled Antibody Biodistribution FIRST Award. NIH - NCI, 12/1/89 - 11/30/93

Principal Investigator, Tc-99m Functional Hepatic Imaging Following Radiation Therapy. Rad Soc N Am. Seed Grant, 1988.

PROJECT CONSULTANT

Targeted Antigen Receptor Treatment of Cancer. Program Project, Memorial Sloan Kettering Cancer Center. Submission June 2005.

Statistical methods for Quantitative Dynamic Imaging in PET with extension to MR and CT. Finbarr O'Sullivan, Ph.D. Irish Health Research Board. December 2004-present

Tumor Infiltrating Lymphocytes in Non-Hodgkin's Lymphoma Treatment. Oliver Press, M.D., Ph.D., July 2001 – present.

Diagnosis of IM Nodal Metastases in Breast Cancer. David Mankoff, M.D., Ph.D., Principal Investigator. July 2001 – present.

PET in Radiotherapy Treatment Planning in head and Neck Cancer. Mentor. David L. Schwartz, M.D., Veterans' Administration Young Investigator Award. Department of Radiation Oncology, 2001.

PET in Sarcoma Soft Tissue Treatment Protocol Development. Mentor. Scott Scheutze, M.D. NIH K08 young Investigator Award. Department of Medical Oncology. 2000-present

PET in Sarcoma Ewing's sarcoma in the Pediatric Population treatment with High Dose Ho-166 DOTMP with Bone Marrow Transplant. Mentor. Douglas Hawkins, M.D. NIH K08 young Investigator Award. Department of Pediatric Oncology. 2000-present

Imaging the Response of Locally Advanced Breast Cancer. NIH/NCI R01. David Mankoff, M.D., Ph.D., Principal Investigator. August 1996 – present.

SimSet: An Imaging Simulation Resource. Tom Lewellen, Ph.D., Principal Investigator. 1995 – present.

Radioiodinated IL-2 for detection of pancreatic insulinitis in pre-diabetes. Carla Greenbaum, M.D., Principal Investigator, 1993 - present.

Pathophysiology of AZT induced myopathy. NIH. Robert Wiseman, Ph.D., Principal Investigator, 1990 - present.

Quantitation of tissue antibody metabolism. DOE, 1988-1990, Oliver Press, Principal Investigator, Fred Appelbaum, Co-Principal Investigator.

Modification of Radiation Induced Vascular Permeability. NCI, 1983-1990. Michael M. Graham, Principal Investigator.

INVITED LECTURES

Western Regional Society of Nuclear Medicine Mid-winter Meeting:
"Treatment of Lymphoma with Radiolabeled Antibodies". Copper Mountain,
Colorado, January 1988.

Second Conference on Radioimmunotherapy and Radioimmunodetection of
Cancer: "Treatment of B-cell Lymphoma with high dose I-131 Monoclonal
Antibody". Princeton, New Jersey, September 10, 1988.

Hematology -Oncology Grand Rounds. "Treatment of Lymphoma with
Radiolabeled Antibodies". University of Colorado Medical Center,
September 19, 1988.

Radiology, Oncology Grand Rounds. "Radioimmunotherapy of Cancer".
University of Nebraska Medical Center. October 20, 1988.

Western Regional Society of Nuclear Medicine Annual Meeting.
"Radiolabeled Monoclonal Antibodies: Therapy". Seattle, Washington,
October 15, 1988.

American Association of Physicists in Medicine Annual Meeting, 1989.
"Review of Clinical Radioimmunotherapy Trials". Memphis, Tennessee,
July 23, 1989.

University of Michigan Division of Nuclear Medicine/Monoclonal Antibody
Group. "Radioimmunotherapy at the University of Washington". Ann Arbor,
Michigan, July 21, 1989.

Society of Nuclear Medicine Western Regional Annual Meeting. "The Future
of Monoclonal Antibodies". Monterey, CA, October 12, 1989.

Western Regional Society of Nuclear Medicine Mid-Winter Meeting.
"Treatment of Prostate Cancer with Sm-153 EDTMP". Copper Mountain,
Colorado, January 22, 1990

Kaiser Permanente Medical Centers of Southern California. Third Annual
Nuclear Medicine Symposium. Radiolabeled Monoclonal Antibodies:
"Diagnostic and Therapeutic Applications in Oncology". Los Angeles, CA,
March 10, 1990.

Fifth International Conference on Monoclonal Antibody Immunoconjugates
for Cancer. University of California, San Diego. "Radioimmunotherapy of B
Cell Lymphoma". San Diego, CA, March 17, 1990.

Sierra Valley Chapter, Society of Nuclear Medicine. "The Future of
Radiolabeled Monoclonal Antibodies". Lake Tahoe, Nevada, April 7, 1990.

Fourth International Conference on Malignant Lymphoma: Current Status and Prospects. "Radioimmunotherapy of B Cell Lymphoma". Lugano, Switzerland, June 9, 1990.

Nebraska Radiological Society, Omaha, Nebraska. "New Directions in Therapeutic Nuclear Medicine". October 17, 1990.

Visiting Professor. University of Nebraska, Department of Radiology. October 17, 1990.

Arkansas Cancer Research Institute NARTI annual guest lecture. August 13, 1991.

Radioimmunotherapy in Germany Conference: "Treatment of B Cell Lymphoma". Stuttgart Germany, October 1992.

Idaho Nuclear Medicine Association: "Fundamentals of Radioimmunotherapy". July 23, 1992.

Immunex Corporation: "Overview of Nuclear Medicine Contribution in Immunology Research". Seattle, Washington, Jan. 12, 1993.

High Country Nuclear Medicine Conference: "Bone Pain Palliation in Prostate Cancer with Sm-153 EDTMP". Vail, Colorado, March 9, 1993.

Pacific Northwest Society of Nuclear Medicine: "Bone Pain Palliation in Prostate Cancer with Sm-153 EDTMP". Portland, Oregon, March 26, 1993.

Western Regional Society of Nuclear Medicine Mid-Winter Meeting: "Bone Pain Palliation in Prostate Cancer with Sm-153 EDTMP". May 1, 1993.

Society of Nuclear Medicine National Meeting: "Fundamentals of Radioimmunotherapy" and "Samarium-153 EDTMP For Treatment of Bone Metastases". June 8, 10, 1993, and June 6, 1994.

Society of Nuclear Medicine Annual Meeting: Update on Sm-153 EDTMP Treatment for Bony Metastases. June 6, 1994.

Washington University Cancer Center Seminar Series: "PET Imaging at the University of Washington. The Clinical/Research Interface." St. Louis, MO, November 21, 1996.

American Association for the Advancement of Science Annual Meeting and Science Innovation Exposition: "Advances in Using Radioisotopes for Cancer Diagnosis and Therapy." Seattle, WA, February 15, 1997.

American Roentgen Ray Society Annual Meeting: "Positron Emission Tomography: Musculoskeletal neoplasms." Boston, MA, May 9, 1997.

Pacific Northwest Chapter, Society of Nuclear Medicine Annual Spring Meeting: “Lymphatic Mapping - Nuclear Medicine.” Vancouver, BC, March 21-22, 1998.

Society of Nuclear Medicine Annual Meeting, Categorical Session: Nuclear Oncology: The Future is Now: “Sentinel Lymph Node Detection in Melanoma and Breast Cancer: The Role of Lymphoscintigraphy.” Toronto, Canada, June 7, 1998.

Japanese Society of Nuclear Medicine Annual Meeting: “Radiolabeled Antibody Therapy of Hematologic Malignancy.” Shikoku, Japan, October 10, 1998.

Western Regional Society of Nuclear Medicine Meeting: “Treatment of Non-Hodgkin’s Lymphoma with I-131 anti-B-Cell Antibodies: Practical Points.” Portland, Oregon, October 25, 1999.

Hamamatsu Hospital and Central Research Laboratory: “PET in Cancer,” “Update in Radiolabeled Antibody Therapy.” Hamamatsu, Japan, September 2000.

Chemotherapy Foundation Symposium XVIII: “High Dose Skeletal Targeted Radiotherapy with Holmium-166 for Multiple Myeloma.” New York, NY. November 6, 2000.

American College of Surgeons Annual Meeting: “Sentinel Lymph Node Imaging.” Chicago, IL. October 24, 2000

University College London, Clinical PET Image Review. London, England, October 31, 2000.

Pacific Northwest Chapter, Society of Nuclear Medicine Meeting. “Clinical PET at the University of Washington.” Ocean Shores, WA, March 30, 2001.

Philip M. Johnson Memorial Lecture. “Cancer Therapy in Nuclear Medicine: Current Concepts and Future Directions.” Columbia University College of Physicians and Surgeons. New York, New York, May 9, 2001.

Columbia University Radiology Resident Grand Rounds. “PET in Sarcoma, a Clinical Model for Cancer Imaging”. New York, New York, May 9, 2001

University of Washington PET Continuing Medical Education Course: Positron Emission Tomography in Oncology. “PET and Tumor Response.” “PET Practice Aspects.” Seattle, WA, May 6-9, 2001, 2002, 2003, 2004.

Chiba University: “PET Imaging in Pediatric Cancer.” Chiba, Japan. June 14, 2001.

Society of Nuclear Medicine Annual Meeting: Special Seminar in PET Response in Cancer Sponsored by the NCI, "PET Imaging Response in Sarcoma." Toronto, Canada, June 22, 2001.

Japanese Society of Nuclear Medicine Annual Meeting:
"Radioimmunotherapy of Non-Hodgkin's Lymphoma, Clinical Reality."
Kanazawa University Medical Center, Japan, October 14, 2001.

New York Academy of Sciences Nuclear Medicine Section: "Recent Developments in Radioimmunotherapy of Non-Hodgkin's Lymphoma." New York, December 12, 2001.

Hawaii Society of Nuclear Medicine Annual Meeting: "Radioimmunotherapy in Non-Hodgkin's Lymphoma" and Cancer therapy with High Energy Emission Bone Seeking Agents". Honolulu Hawaii, February 18 and 19, 2001.

ACR CME "Clinical PET for the Radiologist", March 2003 Two lectures. San Diego, CA: "PET in Lymphoma"; "PET Imaging Response to Treatment"

Japanese Society of Nuclear Medicine, Annual Meeting,
"Radioimmunotherapy in Lymphoma, a Clinical Reality," Kobe, Japan, October 2002,

Biomedical Research Opportunities Workshop, "Hypoxia Imaging Clinical Aspects" Bethesda, MD, 1/31-2/1/03

2002 Conference of the Academy of Molecular Imaging, "Positron Emission Tomography: Imaging Tumor Response". San Diego, CA, October 2002.

UW Mini Med School Lecture Series 2003: "Molecular Imaging and the Imaging Revolution"

West Hawaii Annual Cancer Symposium, "PET in Cancer Clinical Practice", Kona, Hawaii, September, 2003.

PET Center First Anniversary Celebration, "PET and Molecular Imaging Progress and Promise", Porto, Portugal, November, 2003.

A review of Holmium-166 EDTMP therapy in multiple myeloma, Society of Nuclear Medicine Annual Meeting Continuing Medical Education Series. Philadelphia, Pennsylvania, June 21, 2004

"PET Imaging in Breast Cancer" and "New Tracers for PET Imaging Tumor Proliferation" Northeast Regional Society of Nuclear Medicine Annual Meeting, Stamford, Connecticut October 23, 2004

“PET Imaging in Sarcoma Response to Treatment” Connective Tissue Oncology Society Annual International Meeting Montreal, Canada. November 11, 2004.

“ PET Imaging at the University of Washington” Copenhagen University Hospital New PET/CT Center Opening Celebration. Copenhagen, Denmark, April 8, 2005

“PET in Sarcoma, an Overview” Plenary session speaker, .Sarcoma Meeting Stuttgart. Stuttgart, Germany, June 15, 2005.

Session Organizer and Speaker, Society of Nuclear Medicine Annual Meeting Continuing Medical Education Series. Toronto, Canada, June 19, 2005. Two Lectures: Re-defining Tumor Response with Molecular Imaging; FDG PET in Sarcoma: Tumor Risk Stratification and Treatment Planning with FDG PET Imaging.

“PET imaging in Pediatric Bone Tumors” Children’s Cancer Study Group (COG). Dallas, Texas, October 28, 2005.

“ Imaging Response to Targeted Therapy” for GIST. UW/SCCA CME; Solid Tumor Oncology Sept. 28, 2006, Seattle, WA

“Pathology of Sarcoma”. UW Orthopedics Pathology Course. October 21, 2006. Seattle, WA.

“ Imaging Sarcomas”. Pediatric Oncology Imaging Frontiers Workshop”. Sponsored by the NCI. October 23, 2006, Washington D.C.

“Understanding Sarcoma: A PET Imaging Update”. Huntsman Cancer Institute, University of Utah. January 10, 2007

Visiting professor in Nuclear Medicine. “Infection Imaging”. University of Utah Radiology Residency Program January 11, 2007.

“Biology and Imaging of Bone Tumors” Society of Nuclear Medicine Mid-Winter Meeting. February 17, 2007, San Antonio, Texas

“PET imaging in GIST” SWOG GI tumor section, February 24, 2007, Seattle, WA

“PET in sarcoma overview” ICOS at SWOG sarcoma section February 25, 2007, Seattle, WA

“PET in bone tumor imaging” Society of Nuclear Medicine Annual Meeting, Jun 2, 2007, Washington, D.C

“Radiosynovectomy” Society of Nuclear Medicine Annual Meeting, Jun 2, 2007, Washington, D.C

“Understanding Cancer using FDG PET Imaging: the UW sarcoma experience”. Visiting Professor in Nuclear Medicine at the University of Pennsylvania Nuclear Medicine Program, Philadelphia, Pennsylvania. August 23-24, 2007.

“PET in Cancer with Novel Imaging Agents”. ASTRO Molecular Imaging Workshop, San Francisco, California, September 7, 2007

“Imaging in Clinical Trials”/ Schering Corporation molecular imaging and cancer therapy group. Berlin, Germany. October 9, 2007.

“ PET in sarcoma clinical trials” . 2007 CTOS Annual meeting, Seattle, Washington, Friday November 5, 2007.

GRAMEC Grand Rounds, Michigan State University. “FDG PET in Cancer: Understanding Sarcoma”. Grand Rapids, Michigan. June 3-8, 2007

University Cork College, Ireland. “PET in Sarcoma”. August 12, 2008

RSNA Annual Meeting. Refresher course: PET in Sarcoma. Chicago, IL. November 28-29, 2007., December 8, 2009

“PET Imaging of Sarcoma: Role in Management?” 33rd Annual Western Regional Meeting, Western Regional Society of Nuclear Medicine. Portland, Oregon, October 18, 2008.

“PET Imaging in Sarcoma” UW/ Seattle Childrens Rhabdomyosarcoma Conference. Feb 5, 2009, at FHCRC Seattle WA

“Imaging the Tumor Phenotype: The UW PET Sarcoma PET Imaging Experience” Emory University Grand Rounds and visiting Professor, March 10-11, 2009, Atlanta GA.

“Quantitative PET Imaging in Cancer” visiting lecturer, Bayer Pharmaceutial Corp, Imaging Group, November 15, 2010, Berlin Germany

COMMUNITY SERVICE ACTIVITIES

Camp Doctor- fill in support- Camp Sealth , Vashon Island, Puget Sound Campfire Organization. 2005-2007.

PUBLISHED ARTICLES

1. Beamier PL, Krohn KA, Carasquillo JA, Eary JF, Hellström I, Hellström KE, Nelp WB, Larson SM: Melanoma localization in nude mice with monoclonal Fab against p 97. *J Nucl Med* 26(10):1172-1179, 1985.
2. Gilbert BR, Cerqueira MD, Eary JF, Simmons MC, Nelp WB, Nabi HA: In-111 white blood cell scan for infectious complications of polycystic renal disease. *J Nucl Med* 26(11):1283-1286. 1985.
3. Eary, JF, Fisher MC, Cerqueira MD: Idiopathic pulmonary fibrosis: Another cause of ventilation perfusion mismatch. *Clin Nucl Med*: 11(6):396-399, 1986.
4. Beaumier PL, Neuzil D, Yang HM, Noll EA, Kishore R, Eary JF, Krohn KA, Nelp WB, Hellström KE, Hellström I: Immunoreactivity assay for labeled anti-melanoma monoclonal antibodies. *J Nucl Med* 27(6):824-828, 1986.
5. Kishore R, Eary JF, Krohn KA, Nelp WB, Menard TW, Beaumier PL, Hellstrom KE, Hellstrom I: Autoradiolysis of iodinated monoclonal antibody preparations, *J Nucl Med Biol* 13(4):457-459, 1986.
6. Nelp WB, Eary JF, Jones RF, Hellström KE, Hellström I, Beaumier PL, Krohn KA: Preliminary studies of monoclonal antibody lymphoscintigraphy in malignant melanoma. *J Nucl Med* 28(1):34-41, 1987.
7. Badger CC, Eary JF, Brown S, Press O, Davis J, Appelbaum FR, Nelp WB, Krohn K, Miller R, Levy R, Bernstein ID: Therapy of lymphoma with I-131 labeled anti-idiotypic antibodies. *Am Assoc Cancer Res.* 28:388, 1987.
8. Ali SA, Eary JF, Warren SD, Badger CC, Krohn KA. Synthesis and radioiodination of tyramine cellobiose for labeling monoclonal antibodies. *J Nucl Med Biol* 15(5):557-561, 1988.
9. *Eary JF, Appelbaum FL, Durack L, Brown P: Preliminary validation of the opposing view method for quantitative gamma camera imaging. *Med Phys* 16(3):382-387, 1989.
10. Eary JF, Schroff RW, Abrams PG, Fritzberg AR, Morgan AC, Kasina S, Reno JM, Srinivasan A, Woodhouse CS, Wilbur DS, Natale RB, Collins C, Stehlin JS, Mitchell M, Nelp WB. Successful Imaging of Malignant Melanoma with Tc-99m labeled monoclonal antibodies. *J Nucl Med* 30(1):25-32, 1989.
11. Press OW, Eary JF, Badger CC, Martin PJ, Appelbaum FR, Levy R, Miller R, Brown S, Nelp, WB, Krohn KA, Fisher D, Thomas ED, Bernstein ID:

Treatment of refractory non-Hodgkin's lymphoma with radiolabeled MB-1 (anti-CD37) Antibody. *J Clin Oncol* 7(8):1027-1038, 1989.

12. Bianco JA, Sandmaier B, Brown PA, Badger C, Bernstein I, Eary J, Durack L, Schuening F, Storb R, Appelbaum F: Specific marrow localization of an I131 labeled anti-myeloid antibody in normal dogs: effects of a "cold" antibody pre-treatment dose on marrow localization. *Exp Hematol* 17(9):929-934, 1989.
13. Allen MD, Tsuboi H, Togo T, Eary JF, Gordon D, Thomas R, Reichenbach DD: Detection of cardiac allograft rejection and myocyte necrosis by monoclonal antibody to cardiac myosin. *Transplantation* 48(6):923-928, 1989.
14. Ali SA, Warren SD, Richter KY, Badger CC, Eary JF, Press OW, Krohn KA, Bernstein ID, Nelp WB: Improving the tumor retention of radioiodinated antibody: Aryl carbohydrate adducts. *Cancer Res* 50(3 Suppl):783-788s, 1990.
15. Bernstein ID, Eary JF, Badger CC, Press OW, Appelbaum FR, Martin PJ, Krohn KA, Nelp WB, Porter B, Fisher D, Miller R, Brown S. Larry R. Thomas, Ed.: High dose radiolabeled antibody therapy of lymphoma. *Cancer Res* 50(3 Suppl):1017-1021s, 1990.
16. Bianco JA, Brown PA, Durack L, Badger C, Bernstein I, Eary J, Durham J, Fisher D, Sandmaier B, Schuening F, Storb R, Appelbaum A: Effects of propylthiouracil on the biodistribution of an I131-labeled anti-myeloid antibody in normal dogs: dosimetry and clinical implications. *J Nucl Med* 31(8):1984-1989, 1990.
17. *Eary JF, Press OW, Badger CC, Durack L, Richter KY, Addison SJ, Krohn KA, Fisher DR, Porter B, Williams DL, Martin P, Appelbaum FR, Levy R, Brown S, Miller R, Nelp W, Bernstein ID: Imaging and treatment of B-cell lymphoma. *J Nucl Med* 31(8):1257 - 1268, 1990.
18. Press OW, Eary JF, Badger CC, Martin PJ, Appelbaum FR, Nelp WB, Krohn KA, Fisher D, Porter B, Thomas ED, et al: High dose radioimmunotherapy of B-cell lymphomas. *Front Radiat Ther Oncol*, 24:204-213, 1990.
19. Badger CC, Eary JF, Bernstein ID: Fundamentals of immunology and monoclonal antibodies. *Am. Assoc. Phys. Med. Annual Symposium Proceedings*. 6/90.
20. Bianco JA, Brown PA, Wilbur S, Durack L, Badger C, Bernstein I, Sandmaier B, Scheuning F, Eary J, Storb R, Appelbaum FR: Paraiodobenzoyl (PIP) labeling increases the residence time of an Iodine-131 labeled anti-myeloid antibody in a canine model. *J Nucl Med* 31(8):1384-1389, 1990.

21. Badger CC, Davis J, Nourigat C, Wu ZM, Hui TE, Fisher DR, Shulman H, Appelbaum FR, Eary JF, Krohn K, Matthews DC, Bernstein ID: Biodistribution and dosimetry following infusion of antibodies labeled with large amounts of ¹³¹I. *Canc Res* 51:5921-5928, 1991.
22. Eary JF, Durack L, Vanderheyden JL, Williams D, Fritzberg A: Considerations for imaging Re-188 and Re-186. *Clin Nucl Med* 15(12):911-916, 1991.
23. Eary JF: Fundamentals of radioimmunotherapy. *J Nucl Med Biol* 18(1):105-108, 1991.
24. Eary JF: Radioimmunotherapy of B-cell lymphoma. *Annals of Oncology* 2(Suppl 2):187-190, 1991.
25. Eary JF, Nelp WB: Correlative imaging in radioimmunotherapy. *Invest Radiol* 26(8):755-760, 1991.
26. Allen MD, Shoji Y, Fugimura Y, Eary JF, Gordon D, Reichenbach DD: Effects of cyclosporin on the uptake of monoclonal antibody to cardiac myosin. *J Heart Transplantation*. 10(5 Pt 1):775-781, 1991.
27. Matthews DC, Appelbaum FR, Eary JF, Hui TE, Fisher DR, Martin PJ, Durack L, Press OW, Nelp WB, Badger CC, Bernstein ID: Radiolabeled anti-CD45 monoclonal antibodies target hematolymphoid tissue in murine and macaque models. *Antib, Immunocon and Radiopharm.*, 4:713-720, 1991.
28. Mathews DC, Appelbaum FR, Eary JF, Hui TE, Fisher DR, Martin PJ, Durack LD, Nelp WB, Press OW, Badger CC, Bernstein ID: Radiolabeled anti-CD.45 monoclonal antibodies target lymphohematopoetic tissue in the macaque. *Blood* 78(7):1864-1874, 1991.
29. Fisher DR, Badger CC, Breitz H, Eary JF, Durham JS, Hui TE, Hill RL, Nelp WB: Internal radiation dosimetry for clinical testing of radiolabeled monoclonal antibodies. *Antibody Immunoconj Radiopharm* 4(4):655-664, 1991.
30. Bernstein ID, Press OW, Eary JF, Appelbaum FR, Badger CC, Matthews DC, Fisher DR, Martin PJ, Durack L, Levy R, Krohn K, Nelp WB, Thomas ED: Treatment of leukemia and lymphoma using antibody labeled with high doses of ¹³¹I. *Antibodies and Immunoconjugates*. 4:771-776, 1991.
31. Press OW, Eary JF, Badger CC, Martin PJ, Appelbaum FR, Nelp WB, Levy R, Miller R: Radiolabeled antibody therapy of human B-cell lymphomas. *Adv Exp Med Biol* 303:91-96, 1991.
32. Peterson LM, Evans ML, Graham MM, Eary JF, Dahlen DD: Vascular response to radiation injury in the rat lung. *Rad Res* 129(2):139-148, 1992.

33. Hui TE, Fisher DR, Press OW, Eary JF, Weinstein JN, Badger CC, Bernstein ID: Localized beta dosimetry of ¹³¹I-labeled antibodies in follicular lymphoma. *Med Phys* 19(1):97-104, 1992.
34. Appelbaum FR, Badger CC, Bernstein ID, Buckner CD, Deeg HJ, Eary JF, Matthews DC, Press OW, Storb R, Thomas ED: Is there a better way to deliver total body irradiation? *Bone Marrow Transplantation* 10(Suppl 1):77-81, 1992.
35. Appelbaum FR, Matthews DC, Eary JF, Badger CC, Kellogg M, Press OW, Martin PJ, Fisher DR, Nelp WB, Thomas ED, Bernstein ID: The use of radiolabeled anti-CD33 antibody to augment marrow irradiation prior to marrow transplantation for acute myelogenous leukemia. *Transplantation* 54(5):829-833, 1992.
36. Hommeyer SH, Varney DM, Eary JF: Skeletal nonvisualization in a bone scan secondary to intravenous Etidronate therapy. *J Nucl Med*. 33(5):748-750, 1992.
37. van der Jagt RH, Badger CC, Appelbaum FR, Press OW, Matthews DC, Eary JF, Krohn KA, Bernstein ID: Localization of radiolabeled anti-myeloid antibodies in a human acute leukemia xenograft tumor model. *Canc Res* 52(1):89-94, 1992.
38. Pollard KR, Bice AN, Eary JF, Durack LD, Lewellen TK: A method for imaging therapeutic doses of Iodine-131 with a clinical gamma camera. *J Nucl Med* 33(5):771-776, 1992.
39. *Eary JF, Collins CC, Stabin M, Vernon C, Petersdorf S, Baker M, Hartnett S, Ferency S, Addison SJ, Appelbaum FR, Gordon EE: Samarium-153 EDTMP biodistribution and dosimetry estimation. *J Nucl Med* 34(7):1031-1036, 1993.
40. *Press OW, Eary JF, Appelbaum FR, Martin PJ, Badger CC, Nelp WB, Glenn S, Butchko G, Fisher D, Porter B, Matthews DC, Fisher LD, Bernstein ID: Radiolabeled-antibody therapy of B-cell lymphoma with autologous bone marrow support. *NEJM* 329(17):1219-1224, 1993.
41. Collins C, Eary JF, Donaldson G, Vernon C, Bush NE, Petersdorf S, Livingston RB, Gordon EE, Chapman CR, Appelbaum FR: Samarium-153-EDTMP in bone metastases of hormone refractory prostate carcinoma: A phase I/II trial. *J Nucl Med* 34(11):1839-1844, 1993.
42. Press OW, Eary J, Badger CC, Appelbaum FR, Wiseman G, Matthews D, Martin PJ, Bernstein ID: High-dose radioimmunotherapy of lymphomas. *Cancer Treat Res* 68:13-22, 1993.

43. *Eary JF, Pollard KR, Durack LD, Bice AN, Lewellen TK, Matthews D, Press OW, Nelp WB, Appelbaum FR, Bernstein I: Post therapy imaging in high dose I-131 radioimmunotherapy patients. *Med Phys.* 21(7):1157-1162, 1994.
44. Appelbaum FR, Press OW, Matthews D, Eary J, Martin PJ, Bernstein ID: The application of radioimmunotherapy to marrow transplantation. *Bone Marrow Transplantation*, 15(Suppl 1):S188-S192, 1995.
45. *Press OW, Eary JF, Appelbaum FR, Martin PJ, Nelp WB, Glenn S, Fisher DR, Porter B, Matthews DC, Gooley T, Bernstein ID: Phase II trial of 131I-B1 (anti-CD20) antibody therapy with autologous stem cell transplantation for relapsed B cell lymphomas. *Lancet.* 346(8971):336-340, 1995.
46. Matthews DC, Appelbaum FR, Eary JF, Fisher DR, Durack LD, Bush SA, Hui TE, Martin PJ, Mitchell D, Press OW, Badger CC, Nelp WB, Bernstein ID: Development of a marrow transplant regimen for acute leukemia using targeted hematopoietic irradiation delivered by 131I-labeled anti-CD45 antibody, combined with cyclophosphamide and total body irradiation. *Blood* 85(4):1122-1131, 1995.
47. Press OW, Eary JF, Appelbaum FR, Bernstein ID: Myeloablative radiolabeled antibody therapy with autologous bone marrow transplantation for relapsed B cell lymphomas. *Cancer Treat Res.* 76:281-97, 1995.
48. Durack LD, Eary JF: Data collection techniques for pre-radioimmunotherapy imaging. *J Nucl Med Tech.* 23:65-69, 1995.
49. Matthews DC, Appelbaum FR, Press OW, Eary JF, Bernstein ID: Targeted therapy for hematologic malignancies: Has its promise been realized? *Curr Opin Hematol* 2:235-239, 1995.
50. Press OW, Appelbaum FR, Eary JF, Bernstein ID: Radiolabeled antibody therapy of lymphomas. *Important Adv Oncol.* 157-171, 1995.
51. Press OW, Shan D, Howell-Clark J, Eary J, Appelbaum FR, Matthews D, King DJ, Haines AMR, Hamann P, Hinman L, Shochat D, Bernstein ID: Comparative metabolism and retention of Iodine-125, Yttrium-90, and Indium-111 radioimmunoconjugates by cancer cells. *Cancer Res.* 56(9):2123-2129, 1996.
52. Pollard KR, Lewellen TK, Kaplan MS, Haynor DR, Miyaoka RS, Eary JF, Durack LD: Energy-based scatter corrections for scintillation camera images of iodine-131. *J Nucl Med.* 37(12):2030-2037, 1996.
53. Eary JF, Press OW: High dose radioimmunotherapy in malignant lymphoma. *Recent Results Cancer Res.* 141:177-182, 1996.

54. Corcoran MC, Eary J, Bernstein I, Press OW: Radioimmunotherapy strategies for non-Hodgkin's lymphomas. *Annals of Oncology*. 8 (Suppl):S133-S138, 1997.
55. Yuan C, Petty C, O'Brien KD, Hatsukami TS, Eary JF, Brown BG: In vitro and in situ magnetic resonance imaging signal features of atherosclerotic plaque-associated lipids. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 17(8):1496-1053, 1997.
56. Eary JF, Krohn KA, Press OW, Durack L, Bernstein I: Importance of pre-treatment radiation absorbed dose estimation for radioimmunotherapy of non-Hodgkin's lymphoma. *Nucl Med Biol*, 24(7):635-638, 1997.
57. Matthews DC, Appelbaum FR, Press OW, Eary JF, Bernstein ID: The use of radiolabeled antibodies in bone marrow transplantation for hematologic malignancies. *Cancer Treat Res*, 77:121-139, 1997.
58. Mankoff DA, Tewson TJ, Eary JF. Analysis of blood clearance and labeled metabolites for the estrogen receptor tracer, [F-18]-16 α -fluoroestradiol (FES): *Nucl Med Biol* 24: 341-348, 1997.
59. Mankoff DA, Thompson JA, Gold P, Eary JF, Guinee DG, Samlowski WE: Identification of interleukin-2 (IL-2) induced complete response in metastatic renal cell carcinoma by FDG PET despite radiographic evidence suggesting persistent tumor. *AJR*, 169:1049-1050, 1997.
60. Eary JF, Mankoff DA: Tumor metabolic rates in sarcoma using FDG PET. *J Nucl Med*. 39(2):250-254, 1998.
61. Eary JF, Conrad EU, Bruckner JB, Folpe A, Hunt KJ, Mankoff DM, Howlett AT: Quantitative [F-18]Fluorodeoxyglucose positron emission tomography in pre-treatment and grading of sarcoma. *Clin Canc Res*, 4:1215-1220, 1998.
62. Mankoff DA, Shields AF, Graham MM, Link JM, Eary JF, Krohn KA: Kinetic analysis of 2-[Carbon-11]-thymidine PET imaging studies: Compartmental model and mathematical analysis. *J Nucl Med*, 39(6):1043-1055, 1998.
63. Shields AF, Mankoff DA, Link JM, Graham MM, Eary JF, Kozawa SM, Zheng M, Lewellen B, Lewellen TK, Grierson JR, Krohn KA: Carbon-11-thymidine and FDG to measure therapy response. *J Nucl Med* 39(10):1757-1762, 1998.
64. Eubank WB, Mankoff DA, Schmiedl UP, Winter TC, Fisher TC, Olshen AB, Graham, MM, Eary JF: Imaging of oncologic patients: Benefit of joint CT and 18 F-Fluorodeoxyglucose positron emission tomography scan interpretation in the diagnosis of malignancy. *AJR Am J Roentgenol*, 171(4):1103-1110, 1998.

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70. Eary JF, Conrad EU: Positron emission tomography in grading soft tissue sarcomas. *Sem in Musculoskeletal Radiol* 3(2):135-138, 1999.
71. Eary JF: Nuclear Medicine in Oncology Diagnosis. *Lancet*, 354(9181):853-857, 1999.
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74. Minoshima S, Mankoff DA, Heard ME, Eary JF. The current status of clinical PET in the United States. *Innervision* 15(13):92-96, 2000.
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TEXTBOOKS

1. Editor, Nuclear Medicine Therapy. Informa, Inc., New York, London. March 2007.

EDUCATIONAL ACTIVITIES

Eary JF: Antibody Imaging Basic Science. Society of Nuclear Medicine Slide/tape education program - 40 minutes. 1988.

UW/FHCRC Cancer Consortium Molecular Imaging Program
Imaging Workshop chair. November 22, 2004, University of Washington South Campus Center.

Eary JF, *Next-Generation Therapeutic Isotopes* article “Radionuclide Therapy for the Palliation of Bone Metastases.” May 2005.

RSNA 2007-8 Refresher course: PET in Sarcoma

Course Director: University of Washington Molecular Medicine Program:
Conjoint Molecular Medicine/Pathology 514: Molecular Medicine Seminar;
2008-2009

Radiology 693 (Nuclear Medicine) course lecturer and coordinator
2008- present

ABSTRACTS

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**Washington State
Health Care Authority**

Agency Medical Director Comments

**Health Technology Clinical Committee
PET Scan and Lymphoma**

PET and Lymphoma Background

Background: Positron emission tomography (PET) is a diagnostic imaging test using a positron emitting radioactive particle.

- ❑ In using PET for cancer, the radioactive particle is usually 18fluorine (18F) which is incorporated into a glucose molecule.
- ❑ 18FDG preferentially accumulates in areas of high glucose metabolism such as areas of active cancer.
- ❑ 18FDG produces areas of increased radioactivity (referred to as “hot spots”) where cancer cells are metabolically active.
- ❑ Positron emission tomography is frequently performed after other imaging methods, such as CT or MRI, so it may not replace other imaging tests (anatomical vs. biologic)

AMDG Perspective

- ❑ **Technology is not new, but the application is changing**
 - A PET Scan policy was brought forward to the Advanced Imaging Management work group for Medicaid
 - PET is authorized for diagnosis for Lung and GI cancers to abate risky biopsies
 - PET is authorized when conventional scanning (CT, MRI, plain films) are non-diagnostic
 - PET is authorized if lab test and conventional scanning is not congruent (normal scan with increasing CA125 ovarian cancer)
- ❑ **Routine use of PET is not authorized due lack of literature on outcomes**
- ❑ **A key concerns: Will this additional method increase benefits when lesser cost screening has known outcomes?**
 - More expensive/additional test increases costs – what about outcomes?
 - Is the measure of a new test only SN/SP – what about PPV?
 - Is it appropriate to measure PET against CT Scan – anatomic vs. biologic
 - Are there better outcomes or reduced costs for the extra radiation dose?

Current State Agencies Policies

DSHS allows PET when:

There is a Non-diagnostic conventional scan for diagnosis, biopsies, staging/restaging or surveillance

UMP allows PET in lymphoma

SURVEILLANCE OF ASYMPTOMATIC PATIENTS AFTER THERAPY FOR MALIGNANCY PET or PET/CT is considered not medically necessary for patients who have completed therapy twelve (12) or more months ago for lymphoma or six (6) or more months ago for all other malignancies unless the patient demonstrates signs, symptoms, laboratory or other objective findings suggestive of recurrence or spread of the original malignancy

SCREENING: PET or PET/CT IS NOT COVERED AS A SCREENING TEST (I.E., FOR EVALUATION OF PATIENTS WITHOUT SPECIFIC SIGNS AND SYMPTOMS OF DISEASE).

Medicare Policies – see slide 18

State Agencies Questions

- ❑ **Safety: Benefit vs. Harms Issues?**
 - Do less expensive diagnostics have less risk for radiation exposure?
 - Does the identification of non-specific findings (false positives) lead to unnecessary interventions?
 - Is that a Red Flag for over use of PET?
 - ❑ Mode was 1, the mean was 2, and the max per case 19 PET (> 40 CT scans) in 5 year period

State Agencies Questions

□ Effectiveness

- Is the evidence of sensitivity, specificity, and reliability enough to make a benefit decision?
- Can we define when an MRI/CT/Gallium scan vs. PET is needed in a diagnosis, staging/restaging, surveillance?

□ Cost

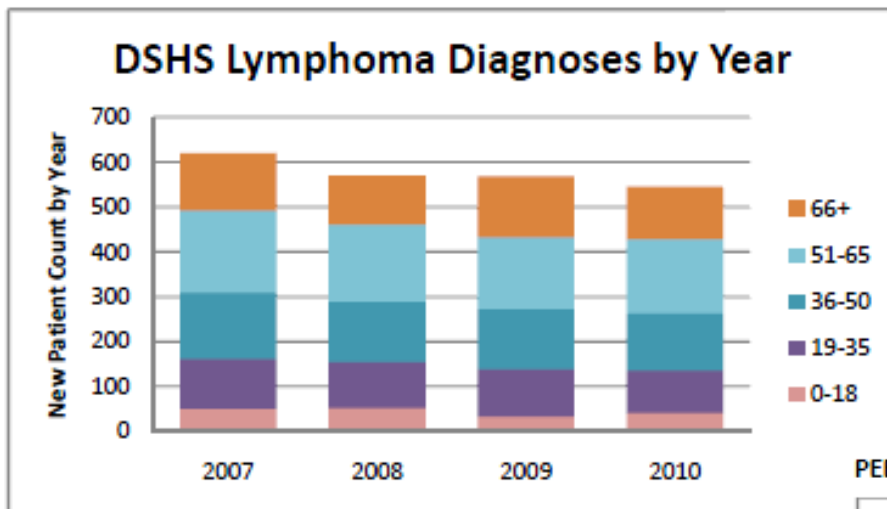
- Does routine PET lead to higher cost for unproven outcomes?
- What is the impact of differential activity in the community (multiple PET and CT Scans per case)?

Codes for PET and CT/PET

Treatments(CPT)			Comparators
			Select all codes
78811-78813	PET scans, Diagnostic nuclear medicine		PET Imaging
78814-78816	PET-CT scan, Diagnostic nuclear medicine		PET Imaging
38790/92/94	Injection for lymph angiography, identification of sentinel lymph node, Cannulation of thoracic duct		Other Imaging - adjunct code: injection/iv of radiopharmaceuticals
78102/03/04	Bone marrow imaging for Lymphatic System (includes gallium scintigraphy), limited area, multiple areas, whole body		Other imaging - Comparator procedure
78800/01/02	Radiopharmaceutical imaging, limited area, multiple areas, whole body		Other imaging - Comparator procedure
78803	Radiopharmaceutical imaging, tomographic (SPECT)		Other imaging - Comparator procedure
78804	Radiopharmaceutical imaging, whole body requiring 2 or more days		Other imaging - Comparator procedure
78808	Injection of radiopharmaceutical by IV for gamma probe study (new code in 2009)		Other imaging - Comparator procedure
76376/7	Interpretation of imaging results, should not be reported with 78811-78816 (new code in 2006)		Other Imaging - adjunct code; additional interpretation charge for non PET imaging
71250/60/70	Computed tomography (CT), thorax; without contrast material/ with contrast material/ with and without contrast		Other imaging - Comparator procedure
74150/60/70	CT of the Abdomen w/o, w, w/o and w contrast		Other imaging - Comparator procedure

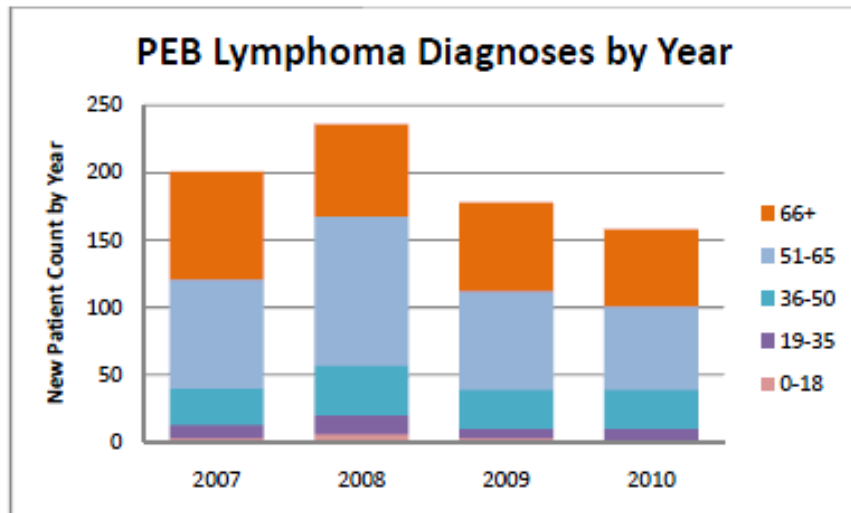
Cost and Utilization for PET and CT/PET by Year

DSHS Lymphoma Diagnoses by Age and Year



Note: May include new members with a pre-existing condition.

PEB Lymphoma Diagnoses by Age and Year



Note: May include new members with a pre-existing condition.

Cost and Utilization for PET and CT/PET

PEB PET Scans, Costs and Counts for patients diagnosed with Lymphoma 2007-2010

PEB PET Scans	2007	2008	2009	2010	Overall
Members w/PET scans /yr	140	168	161	148	409
Scans per year	221	263	246	235	965
Average scans per year**	1.58	1.57	1.53	1.59	2.36
Annual Cost	\$489,106	\$744,611	\$605,527	\$612,285	\$2,451,529
Average overall cost	\$2,213	\$2,831	\$2,461	\$2,605	\$2,540
Average Primary Payer cost	\$3,421	\$3,876	\$3,756	\$3,797	\$3,735

DSHS PET Scans, Costs and Counts for patients diagnosed with Lymphoma 2007-2010

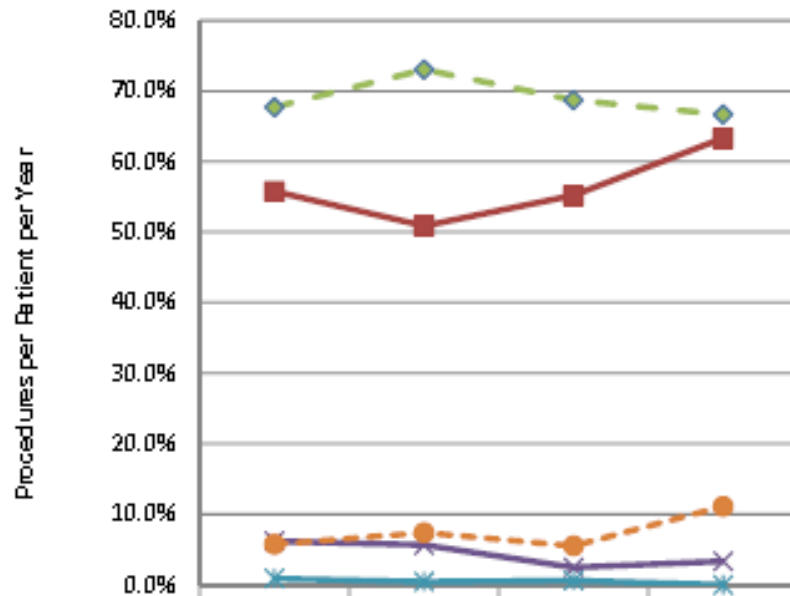
DSHS PET Scans	2007	2008	2009	2010	Overall
Members w/ PET scans per yr	149	178	192	92	611
Scans per year	198	240	263	113	814
Average scans per year	1.33	1.35	1.37	1.23	1.33
Annual Cost	\$151,470	\$196,394	\$205,563	\$87,697	\$641,124
Average scan cost	\$765	\$818	\$782	\$776	\$788

**Average number of scans for all patients who had PET scans during the year

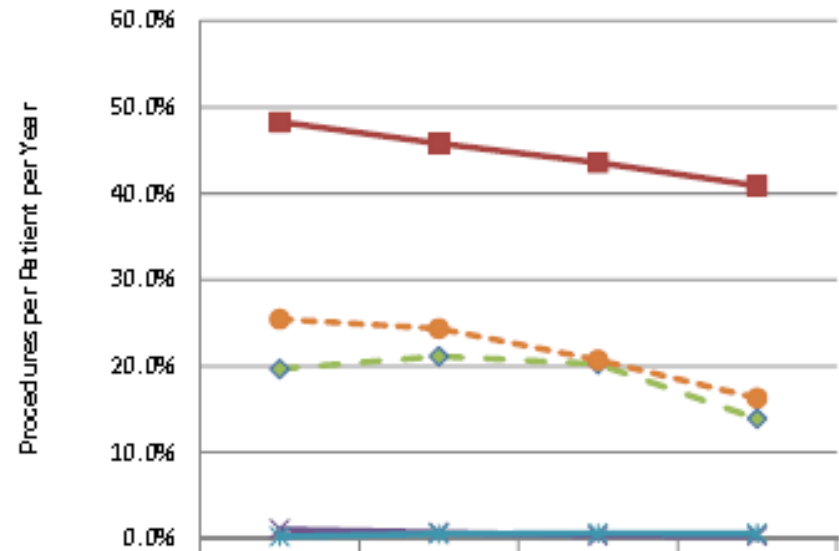
Cost and Utilization for PET and CT/PET

PEB Lymphoma Test Use Pre and Post Diagnosis

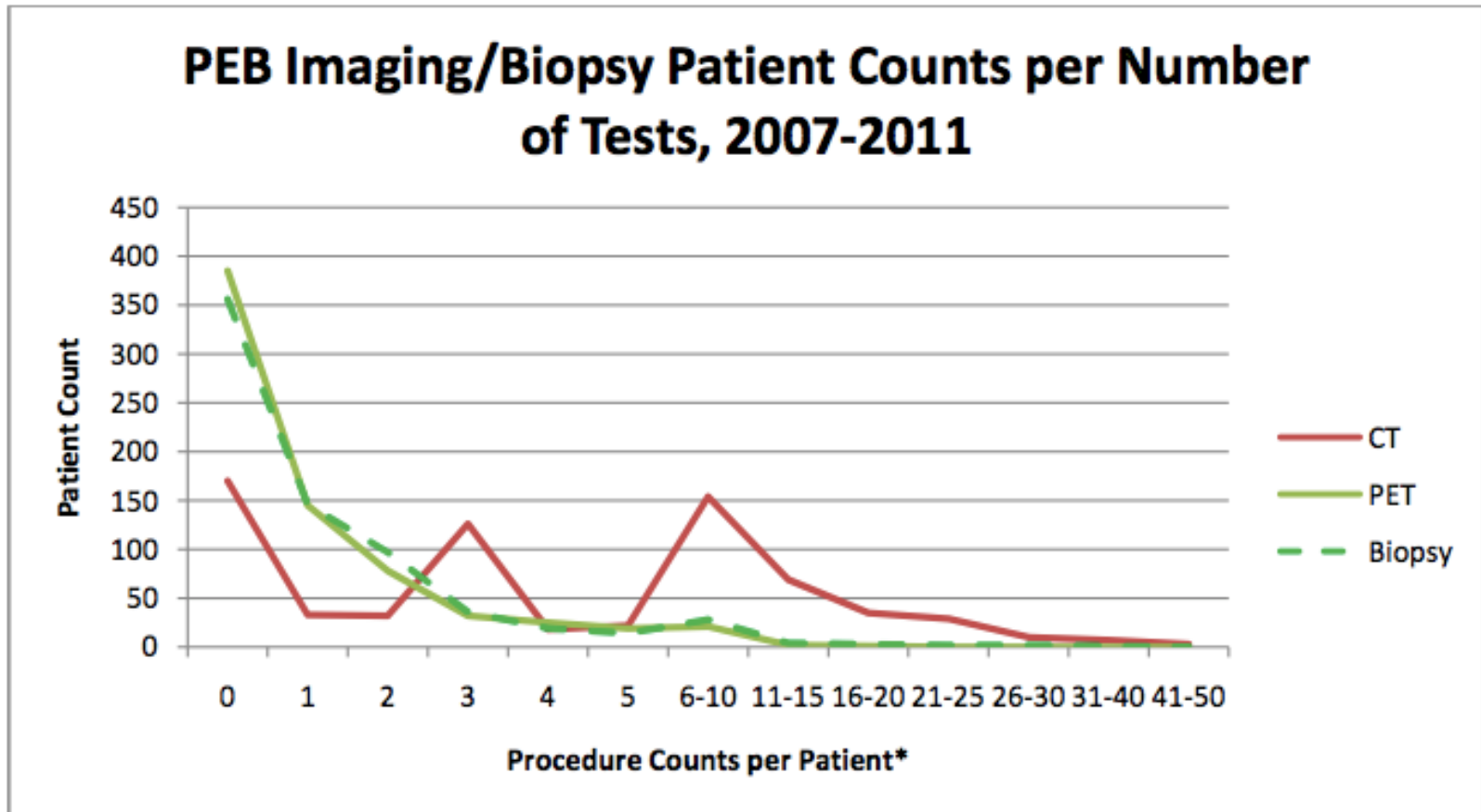
**PEB Lymphoma Patients Pre-diagnosis
Percent of Patients by Test Type**



**PEB Lymphoma Patients Post-diagnosis
Percent of Patients by Test Type
(Lymphoma Diagnosis Code Procedures only)**



PEB Lymphoma Patient Counts by number of Tests, 2007-2011

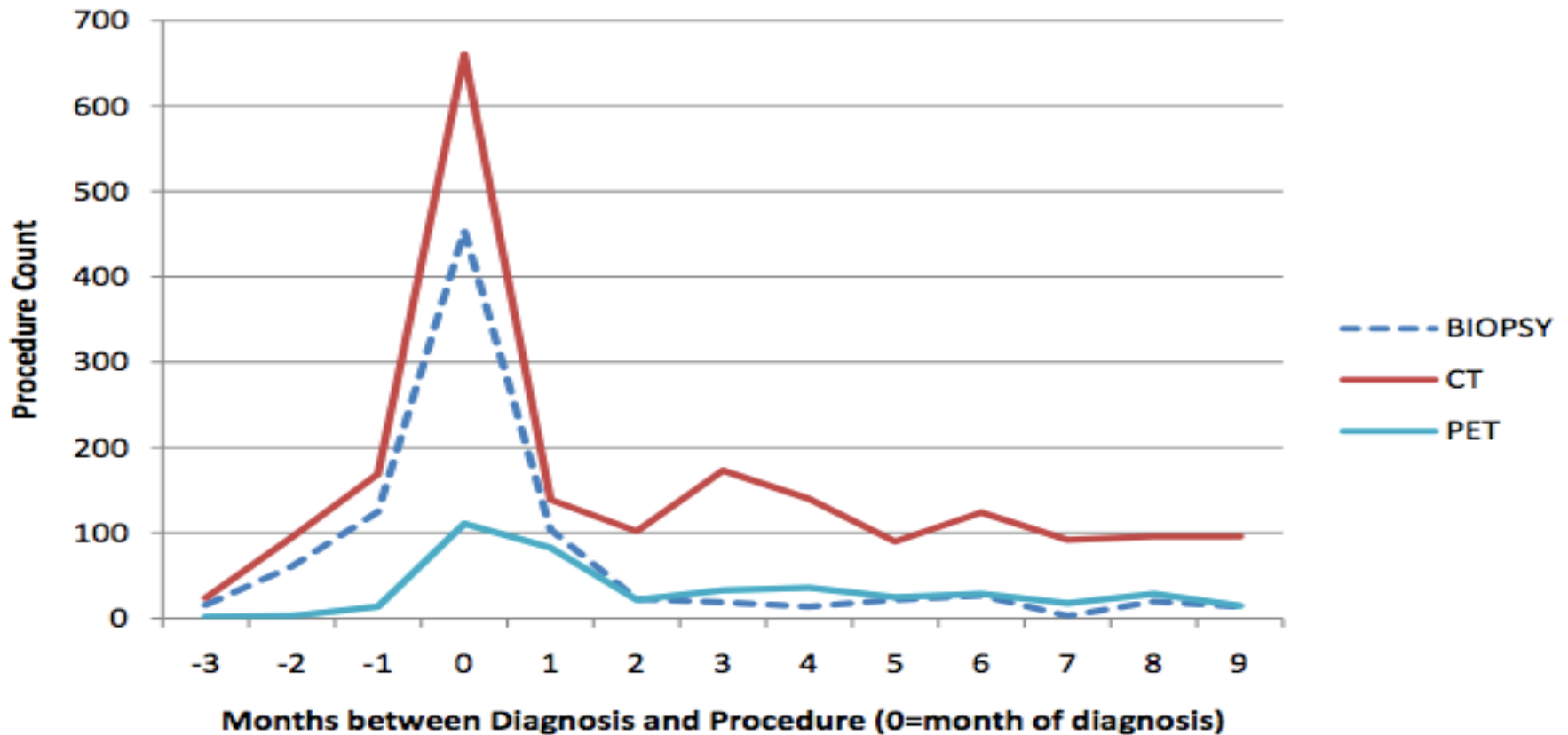


**Patients with a "0" procedure count may include short term members and those at the end of a continuum of treatment in 2006.*

State Agency Utilization (2007-2010)

PEB Lymphoma Visualization Timing Relative to Diagnosis, 2007-2010

PEB Lymphoma Imaging/Biopsy Timing Relative to Diagnosis, 2007-2010



PEB Lymphoma Patient PET Scan Summary Statistics

PEB Lymphoma Diagnosis Code PET Scans, Consolidated 2007-2010

PET Scan in Lymphoma Summary	Hodgkins Lymphoma Patients	Non-Hodgkins Lymphoma Patients	All Lymphoma Patients
PET Scan Count	180	613	793
Patient Count	61	262	323
Average # scans/patient	2.95	2.34	2.46
Median scan count	2	2	2
Maximum scan count	15	19	19
Mode	1	1	1
Std Dev	2.54	2.14	2.23

Note: Table 5a includes PET scans with a Lymphoma diagnosis code only

Brief report

Pretransplantation functional imaging predicts outcome following autologous stem cell transplantation for relapsed and refractory Hodgkin lymphoma

Alison J. Moskowitz,¹ Joachim Yahalom,¹ Tarun Kewalramani,² Jocelyn C. Maragulia,¹ Jill M. Vanak,¹ Andrew D. Zelenetz,¹ and Craig H. Moskowitz¹

¹Lymphoma Service of the Division of Hematologic Oncology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY; and
²Hematologic Malignancies, Lahey Clinic Medical Center, Burlington, MA

To identify prognostic factors for patients transplanted for relapsed or refractory Hodgkin lymphoma we carried out a combined analysis of patients followed prospectively on 3 consecutive protocols at Memorial Sloan-Kettering Cancer Center. One hundred fifty-three patients with chemosensitive disease after ICE (ifosfamide, carboplatin, and etoposide)-based salvage therapy (ST) proceeded to high-dose chemoradiotherapy followed by au-

tologous stem cell transplantation (ASCT). Patients were evaluated with computed tomography and functional imaging (gallium or fluorodeoxyglucose-positron emission tomography) prior to ST and again before ASCT. Functional imaging status before ASCT was the only factor significant for event-free survival (EFS) and overall survival by multivariate analysis and clearly identifies poor risk patients (5-year EFS 31% and 75% for

FI-positive and negative patients respectively). Administration of involved-field radiotherapy with ASCT was marginally significant for EFS ($P = .055$). Studies evaluating novel STs, conditioning regimens, post-ASCT maintenance, or allogeneic stem cell transplantation are warranted for patients who fail to normalize pre-ASCT functional imaging. (*Blood*. 2010;116(23):4934-4937)

PET and Lymphoma: Other Centers, Agencies and HTAs

□ *Hayes Inc.* (07)

■ Hodgkin's lymphoma (primary staging)

- **B** and in patients with biopsy-proven recurrent Hodgkin's disease or non-Hodgkin's lymphoma (restaging):
 - **B** - for FDG PET as an adjunct to standard staging techniques, including
 - laparotomy, CT, x-ray, MRI, US, and bone scan, when used as **an alternative to gallium scanning**;
 - **B** - for FDG PET when used as a guide to limited or directed biopsy, imaging, or visualization for evaluation of a particular lesion,
 - when used as an **alternative to gallium scanning**;
 - **C** - for standard staging techniques or a guide to limited or directed staging methods for evaluation of a particular lesion. For PET when used as an early method for monitoring the effects of therapy and altering treatment accordingly:
 - **C** - for patients with Hodgkin's disease or non-Hodgkin's lymphoma when used as a method for tumor grading when the presence of primary or recurrent tumor is known:

■ **C for FDG PET non-Hodgkin's disease.**

■ **C.** for FDG PET with any image analysis method for differentiating lymphomatous from nonmalignant CNS lesions in patients with HIV infection or AIDS:

■ **D** for all other applications

PET and Lymphoma: Other Centers, Agencies and HTAs

- ***Centers for Medicare & Medicaid Services (CMS):***
 - CMS issued a decision not to make a national coverage decision (NCD) for PET scanning in malignancies. This leaves ultimate coverage decisions on 18FDG PET to local Medicare carriers. In the Decision Memo, CMS (2010) created a two-part framework for analysis of PET use in malignancies—initial treatment strategy and subsequent anti-tumor strategy.(CMS, 2010).
 - For Initial Treatment Strategy, CMS will “nationally” cover lymphoma and other solid malignancies for one FDG PET study for determining the optimal location to perform an invasive biopsy and to determine stage of the tumor
 - Moreover, CMS allows local Medicare contractors to make local decisions for coverage of additional PET scans for therapeutic purposes related to initial treatment strategy.
 - For Subsequent Anti-tumor Treatment Strategy, lymphoma is considered separately from other malignancies. Positron emission tomography is covered without exception.

PET and Lymphoma : Other Centers, Agencies and HTAs

□ Group Health

- Diagnosis: PET results may assist in determining the optimal location to perform an invasive diagnostic procedure. It is not covered for other diagnostic uses or screening (testing patients without symptoms).
- Staging and re-staging: PET is covered when staging remains in doubt after conventional staging and when clinical management of the patient would differ depending on the stage of lymphoma. Re-staging includes re-staging in the setting of recurrence and restaging following completion of a treatment regimen.
- Monitoring of therapy: PET is NOT covered.

- Imaging in Early-Stage Hodgkin's Lymphoma N Engl J Med 2010; 362:962 [March 11, 2010](#)

Data on exposure to low-dose ionizing radiation from medical imaging procedures indicate that medical imaging can potentially harm patients if the cumulative radiation dose becomes excessive.¹ This concern, in conjunction with the present environment of high medical costs, makes it important to identify practices in which it is prudent to eliminate medical imaging that is neither cost-effective nor beneficial. There is a good case for eliminating unnecessary imaging in patients with non-bulky early-stage Hodgkin's lymphoma. **Not only is the recurrence rate 10% or less with the best standard of care, but also approximately 80% of these recurrences are first identified by the patient or the examining physician without the use of imaging. This means that the addition of serial post-therapy imaging provides “earlier” disease detection in only about 2% of treated patients, with no proven benefit.** Yet these patients, who are usually young, generally undergo 5 to 10 episodes of surveillance computed tomography (CT) of the chest, abdomen, or pelvis, often in addition to several episodes of positron-emission tomography (PET)–CT, within the initial 3 to 5 years of their treatment, resulting in an effective cumulative dose of over 50 mSv. Physicians should therefore question the use of imaging studies in these patients beyond those performed for assessment of a response or for clear-cut cases in which management decisions must be guided by imaging. At the most, yearly chest radiography, which is associated with a considerably lower radiation dose than CT or PET-CT, should be performed in patients with previous mediastinal disease. **Any imaging beyond that is not only unjustified but also potentially harmful.**

TABLE 2: Radiation Doses From Common Imaging Studies

Test	Dose (mSv)	Equivalent Period of Background Radiation	Reference
Chest x-ray (standard two views)	0.06–0.1	8–12 days	13, 14
Mammography	0.13–0.7	16–88 days	13, 14
Abdomen x-ray	0.5–0.7	62–88 days	14
Lumbar spine x-rays	1.8	7 months	14
Head CT	2.0	8 months	13
Chest CT	8.0	3 years	13
Abdomen and pelvis CT	10.0	3 years	13
Virtual colonoscopy	10.2	3 years	15
Whole-body PET/low dose CT	8.5–10.3	3 years	16
Whole-body PET/full dose CT	23.7–26.4	8–9 years	16
Prospective ECG-gated coronary CT angiography	3.0	1 year	17
Retrospective ECG-gated coronary CT angiography	11.7–13.0	4 years	17
Coronary angiography (diagnostic)	4.6–15.8	2–5 years	14
Coronary angiography (with intervention)	7.5–57.0	2–19 years	14

CT Radiation Dose: What Can You Do Right Now in Your Practice? AJR:196, March 2011 619 -624

State Agencies Summary View

- ❑ PET in Lymphoma
 - Improved Sen/Spe but not related to PPV
 - No better than convention Gallium
 - State policy allows PET after conventional scanning is shown non-diagnostic
- ❑ Safety Issues not resolved
 - Increased amounts of radiology for questionable outcomes
- ❑ Costs Issues
 - Added cost but no outcome data
 - Costs Effectiveness studies – none available

■ State Agencies Summary View

- Non cover for routine diagnostic
 - Cover for biopsies when conventional not adequate
 - For all other reasons (i.e. staging, restaging, surveillance) cover only when conventional scans are non-diagnostic
- Limit the number of scans to no more than 1 per year unless medically justified

?Questions?



PET for Lymphoma

Washington Health Technology Assessment Program

Presented by: Edgar E. Clark, MD, MHA

Date: September 16, 2011

Introduction

- Background
- Key Questions
- Methods
- Findings
- Guidelines
- Summary

Background: Lymphoma

- Heterogeneous group of malignancies involving lymph nodes, bone marrow, spleen and other extra-lymphatic organs
- Approximately 74,000 cases in US annually
 - Hodgkin lymphoma (HL) ~ 13%
 - Non-Hodgkin lymphomas (NHL) ~ 87%

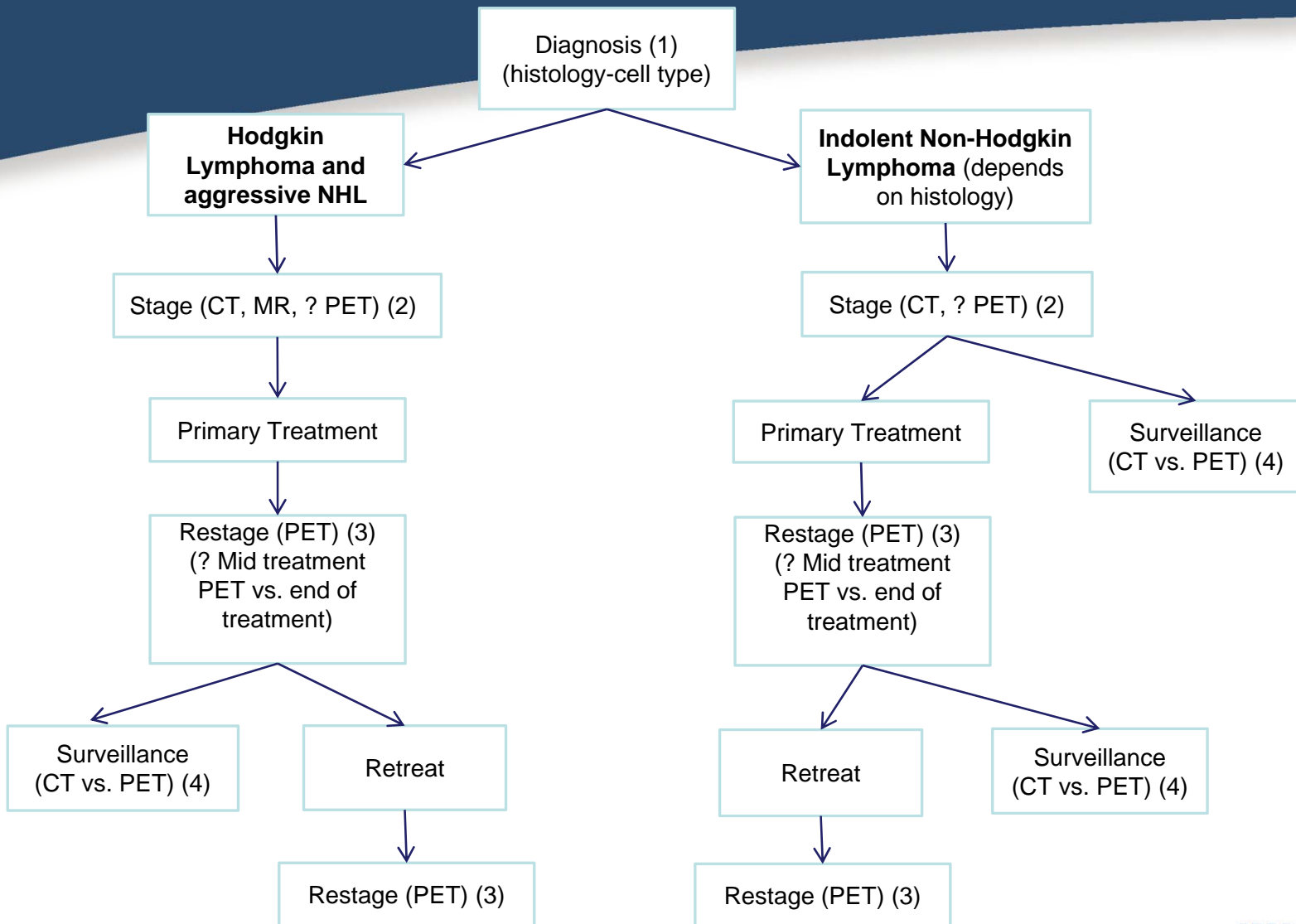
Background: Lymphoma

- HL = classic (95%) and nodular lymphocyte predominant (5%)
- NHL = B-cell (80%) and T-cell (20%) lymphomas
- NHL = aggressive (aNHL), indolent (iNHL) and highly aggressive

Background: Lymphoma

- Treatment: Chemotherapy, radiation therapy or combination chemo-radiation
- Treatment dependent on cell type and on stage of lymphoma
- Primary treatment may result in remission; if lymphoma progresses or recurs, secondary treatment is undertaken

Clinical Management Algorithm



Background: Lymphoma

In this report, Monitoring = assessment that occurs during the course of treatment rather than at the conclusion of treatment.

For iNHL, treatment may be delayed in favor of observation.

Background: Lymphoma

This report investigates role of PET in HL, aNHL and iNHL for the following indications:

- Screening and diagnosis
- Initial staging prior to treatment
- Restaging after primary and secondary treatment
- Estimation of prognosis after treatment
- Surveillance
- Monitoring of treatment during treatment

Background: PET

- Nuclear Medicine test using a positron emitting radionuclide fluorine 18 (^{18}F)
 - Positrons annihilate with electrons resulting in two gamma photons detected by the scanner
- ^{18}F incorporated into a glucose analog (^{18}FDG) and injected intravenously
- ^{18}FDG accumulates in areas of high glucose metabolism
- PET results in “hot spots” where glucose metabolism is high— e.g. cancer, infection

Background: PET

- PET uses abnormal glucose metabolism rather than changes in normal anatomy and tissue characteristics (e.g. CT and MRI) to detect cancer
- In this report, PET always refers to ^{18}F FDG PET
- **Claim:** PET more sensitive and specific than CT or MRI for detecting viable cancer
 - E.g. residual mass in mediastinum after primary treatment for HL; is it residual fibrous tissue or viable HL?

Background: PET

- PET images have low spatial resolution
- PET usually performed with CT in a fusion PET/CT scanner that gives metabolic and high spatial anatomic information synchronously
- In this report PET and PET/CT are considered as one test
 - Older literature is PET alone; newer literature is PET/CT

Background: Washington experience

- Lymphoma incidence
 - PEB: 150-230 cases per year
 - DHHS: 530-610 cases per year
- PET utilization
 - PEB: 220-263 PET scans per year
 - DHHS: 113-263 PET scans per year
- PET costs
 - PEB: \$2,213-\$2,831 per scan
 - DHHS: \$765-\$818 per scan

PICO

- **Population:** Adults and children with Hodgkin lymphoma and non-Hodgkin lymphoma.
- **Intervention:** PET (PET/CT)
- **Comparator:** MRI, CT, gallium, other imaging methods
- **Outcomes:** Comparative diagnostic performance; effects on clinical decision making; effects on patient outcomes, safety and costs.
 - screening and initial diagnosis,
 - initial staging,
 - restaging after primary treatment,
 - detection of recurrence,
 - predicting patient outcomes after primary or secondary treatment,
 - monitoring of response to treatment, and
 - surveillance of patients in remission

Key Questions

- 1. What is the evidence of accuracy of PET (alone or combined on one system with CT—PET/CT) imaging for known or suspected lymphoma compared to CT, MRI, gallium, other diagnostic methods?**

Key Questions

- 2. What is the evidence of clinical effectiveness of PET imaging in patients with known or suspected lymphoma compared to CT and MRI when used as an adjunct to CT or MRI or Gallium, including:**
- Reduced need for other tests or less invasive test
 - Change in patient management (e.g. continuation of chemotherapy)
 - Improvement in quality of life
 - Reductions in morbidity and mortality

Key Questions

- 3. What is the evidence that PET imaging in patients with known or suspected lymphoma has differential efficacy or safety issues in sub populations?**
- Patient age, gender, patient selection criteria
 - Type of scanning machine, software, training
 - Provider type, setting
 - Health care system type

Key Questions

4. What is the safety profile of PET for patients with lymphoma?

- Adverse events type and frequency (mortality, major morbidity, other)

5. What is the evidence about the cost impact of PET for patients with lymphoma?

- Costs in short term
- Costs in long term

Methods

- For the WA HTA program, MED core sources searched for SRs, MAs, TAs from 2000 to 2011. MEDLINE search for 2009-2011 included SRs, MAs, TAs and case reports. Search terms *positron emission tomography, PET, lymphoma, Hodgkin disease*.
- Search for relevant clinical practice guidelines using MED core sources and Guidelines.gov databases
- Quality of included systematic review and guidelines rated with standard MED instruments
- State, private payers, and policy websites searched to identify insurance coverage policies

Search Results

- Core source search yielded 7 SRs and TAs, 3 cost or cost-effectiveness study designs and 6 clinical practice guidelines
- MEDLINE search yielded 354 citations from which 18 observational studies were included in this report

Findings: Evidence presented by lymphoma type

- Hodgkin disease (HL) and aggressive non-Hodgkin disease (aNHL) are combined
- Indolent non-Hodgkin disease (iNHL) is considered separately
- Highly aggressive non-Hodgkin disease – no evidence identified

Findings: Overview

- Primary evidence comes from case series
 - Case series considered to be lower strength of evidence than RCTs or cohort studies
- SOE for most KQs is low to moderate even when SRs are of high quality
- More evidence for diagnostic accuracy than for clinical effectiveness, safety, cost
- More evidence for HL and aNHL than for iNHL

KQ1: Accuracy of PET vs. CT, MRI, gallium for HL and aNHL

- Screening and initial diagnosis
- Initial staging
- Restaging after primary and secondary treatment
- Estimation of prognosis after primary or secondary treatment
- Monitoring of response to treatment (during treatment)
- Surveillance of patients in remission

Accuracy of PET: Screening and initial diagnosis

- No evidence on use of PET for screening or initial diagnosis
- Diagnosis requires histology; PET cannot eliminate biopsy
- No guidelines support PET for these indications

Initial staging

- Australian MSAC TA (4 SRs)
- As a separate test, PET has higher combined sensitivity and specificity than CT or gallium

Test	Sensitivity	Specificity
PET	88-100%	90-100%
CT	88%	80%
Gallium	29-93%	n/a

- As an incremental test (added to CT), two small series of 33 and 50 patients (from Australian MSAC):
 - PET increased the number of true and false positives (ratio of TP: FP = 3:1).
 - PET occasionally was negative at sites positive on CT; large portion of these negative PET scans were false negatives.

Staging after primary treatment

Routine (Four SRs):

- Evidence is heterogeneous, mixing HL and aNHL, initial and post-treatment staging CT
 - PET has higher sensitivity and specificity for detection of HL and aNHL than CT

Modality	Sensitivity	Specificity
CT (Kwee) (mixed HL and aNHL)	25-100%	42-67%
PET (Kwee)	71-100%	57-100%
PET/CT (Kwee)	91-100%	87-100%
PET meta-analysis (Terasawa)	84% (HL) 72% (aNHL)	90% (HL) 100% (aNHL)

Staging after primary treatment

- Evaluation of residual mass (3 SRs):
 - Sensitivity and Specificity for PET ranges 40-100%
 - Both sensitivity and specificity important in clinical decision making about a residual mass
 - Sensitivities and specificities of 40% may not be sufficiently high for clinical decision making

Estimation of prognosis after treatment

- After primary or secondary treatment responders (PET negative) proceed to surveillance and non-responders (PET positive) proceed to additional treatment
- After **primary** treatment, 2 small case series (99 and 127 patients): PET performed and compared with 2-3 year progression free survival (PFS)

Modality	2-3 year PFS if study negative (responder)	2-3 year PFS if study positive (non-responder)
PET (HL)	94-96	19-33
CT (HL)	90	0%
PET (aNHL)	87	7%
CT (aNHL)	63%	0%

Estimation of prognosis after secondary treatment

- Two SRs and three case series
- PET done prior to salvage chemotherapy and stem cell transplant

Study	Population	Sensitivity	Specificity	Other
Terasawa (SR/MA)	HL and aNHL	69%	81%	LR + 3.6 LR - 0.38
Poulou (SR/MA)	HL and aNHL			HR + 3.23
Moscowitz (153 pts)	HL	50%	84%	HR + 3.4
Dodero (80 pts)	HL and aNHL	68%	63%	
Qaio (34 pts)	aNHL	75%	87%	PPV 86%
				NPV 76%

Surveillance of asymptomatic patients

- Surveillance = routine study of patients without symptoms
- Not the same as re-evaluation of patients with clinical evidence of progression such as progressive symptoms, new or increasing lymphadenopathy or other masses

Surveillance of asymptomatic patients

- No SRs or RCTs; 5 case series
- Studies consistently show a high false positive rate for PET scans performed on asymptomatic patients
- PPVs 23-54%; NPVs 90-100%
- Clinical symptoms were effective in predicting relapse

Monitoring of treatment during treatment

PET advocated in mid-cycle of treatment (e.g. after 4 of 8 cycles of chemotherapy)

- Rationale # 1: if PET can predict non-response in mid-cycle, initial treatment could be terminated and secondary treatment begun, saving the expense and side effects of additional cycles of primary treatment.

Need high PPV or LR + for PET

- Rationale # 2: if PET showed response in mid-cycle, *perhaps* no additional treatment needed; *perhaps* stop at 4 cycles. **Need high NPV or low LR - for PET**

- No evidence to support this rationale

Monitoring of treatment during treatment

One SR/MA and 3 case series

Study	Population	Sensitivity	Specificity	Other
Terasawa (SR/MA)	HL (360 pts) NHL (311 pts)	81% 78%	97% 87%	LR+ 28 LR- 0.19 LR+ 5.9 LR- 0.26
Zinzani (91 pts)	aNHL	82%	89%	PPV 82% NPV 89%
Markova (50 pts)	HL	75%	100%	PPV 75% NPV 100%
Duhrsen (128 pts)	aNHL	n/a	n/a	PET +, recurrence rate 17% PET -, recurrence rate 3%

Monitoring of treatment during treatment

- Studies consistently show higher specificity (87-97%) than sensitivity (78-81%)
- NPVs are higher than PPVs
- LR – are stronger than LR +
- PPV, NPV, LR + and LR – may not be strong enough to change clinical decision making

KQ2: Clinical Effectiveness for HL and aNHL

- No evidence on the effect of PET on
 - Reduction of use of other tests
 - Patient survival
 - Quality of life
- Limited evidence of effect of PET on
 - Changes in management

KQ2: Clinical Effectiveness for HL and aNHL

Changes in clinical management:

- Australian MSAC TA
 - No direct evidence
 - Staging alters clinical decisions
 - Monitoring could alter clinical decisions
- Pommier (case series of 137 patients)
 - 137 HL patients; 124 patients scheduled for radiotherapy had PET:
 - 102 (82%) had no change in plan; 6 (5%) had radiotherapy cancelled; 16 (13%) had radiotherapy plan altered

KQ1: Accuracy of PET in Indolent NHL (iNHL)

- Evidence on iNHL is very heterogeneous—different studies report on different iNHLs which do not necessarily behave similarly; individual case series for each iNHL; no MAs or RCTs; reference standard in these studies often not stated; analyses mix patients and lymphoma sites
- Strength of evidence is LOW

Original Diagnosis and Staging

- No evidence on diagnosis
- PET appears to detect additional sites of disease not detected on CT but PET also misses disease sites identified on CT
- One study (Fueger) reported that PET/CT had higher sensitivity (99%) than the individual components PET (68%) and CT (70%) for detection of lymphoma sites

Estimation of prognosis after treatment

No SRs, MAs; 2 small case series of 45 and 44 patients

- PET evidence of nodal activity after treatment correlated with subsequent relapse $p < 0.05$
- PET had a sensitivity of 100% and specificity of 88% for predicting relapse at one year.
PPV = 62%; NPV = 100%

KQ2: Changes in management

One case series (74 patients with mantle cell lymphoma)

- Treating physicians asked for management plan blinded to PET results
- Management plans before and after PET results
 - No change 7%; small change 59%; medium change 7% and large change 27%

KQ3: Differences in sub-populations

No evidence for any differences in sub-populations

- Patient age, gender, patient selection criteria
- Type of scanning machine, software, training
- Provider type, setting
- Health care system type

KQ4: Safety of PET in patients with lymphoma

Australia MSAC considers PET to be safe and not different for lymphoma than for other indications for PET

- This is an editorial opinion
- No direct evidence

KQ4: Safety of PET in patients with lymphoma

Potential safety issues

- Contrast reaction to ^{18}F FDG
 - Glucose analog; no reactions reported
- Radiation dose significant but patients have a potentially fatal disease
 - Radiation dose considerations more important in HL (mostly younger patients) and in surveillance (multiple PETs in potentially cured patients)
- Incidental findings: no evidence on rate of incidental findings but a number of false positive PETs reported

Radiation dose

- Radiation dosage
 - PET: 10-30 mSv (~300 CXRs)
 - Standard CT: 10-30 mSv (~300 CXRs)
 - Low dose CT: 2-10 mSv (~100 CXRs)
 - PET/CT: 12-60 mSv (potentially 600 CXRs)
- ACR estimates the additional lifetime risk of fatal cancer from 30 mSv to be “moderate” (risk = 1/1,000 to 1/500)

KQ5: Costs of PET

Evidence is weak

- Different health delivery systems and costs
- Australian MSAC (2010). Economic model using PET for staging estimated savings of A \$150-210 per patient with PET
- 130 HL in Brazil, PET used for staging if CT inconclusive; savings of 1% overall for HL
- 192 HL in US; PET and CT used for surveillance; US \$100,000 and 147 mSV per recurrence detected
- 68 HL and aNHL in Switzerland with PET at mid-treatment and again at end of therapy; if PET at mid-treatment was negative, could avoid PET at end of treatment with a savings of 26% on PET costs

Guidelines

- Six guidelines included in report:
 - CADTH (2010)
 - IHPL(2007)
 - NCCN (2011 and 2011)
 - ACR (2010 and 2011)
- Guidelines quality rated as poor (IHPL) to fair (NCCN, ACR) to good (CADTH) based primarily on systematic literature review and author independence

Guidelines

Guideline	CADTH	NCCN HL	NCCN NHL	Juweid (IHPL)	ACR HL F/U	ACR HL Stage I-II
Diagnosis	Not addressed	Not addressed	Not addressed	Not addressed	Not addressed	Not addressed
Primary staging	Recommend	Recommend	Optional	Recommend	N/A	N/A
Secondary staging	Recommend	Recommend	Not recommend	Recommend	N/A	N/A
Estimate prognosis	Some reports suggest value	Recommend	Not recommend	Recommend if results will alter management	N/A	N/A
Monitor treatment	Not addressed	Not addressed	Not addressed	Not addressed	Not addressed	Not addressed
Surveillance	Not recommend	Not recommend	Not recommend	Not recommend	Not recommend	Not recommend

Policy Considerations

- Coverage policies for Medicare, Regence Blue Cross, Aetna and Group Health
- CMS Decision Memo (2010): CMS did NOT issue a national coverage decision
- CMS (2010) has a new PET framework:
 - Initial treatment strategy: NCD of one PET
 - Subsequent anti-tumor treatment strategy: left to local regional carriers to decide
 - Exception for lymphoma– cover all PET

Policy Considerations: Insurance Coverage

Indication	CMS	Aetna	Blue Cross	GroupHealth
Diagnosis	Cover to determine optimal location for biopsy	Cover to determine optimal location for biopsy	Cover to determine optimal location for biopsy	Cover to determine optimal location for biopsy
Staging and re-staging	Cover one PET for initial staging; subsequent staging unlimited (NCD)	Cover	Cover	Cover
Monitoring of treatment	Cover if necessary to determine optimal treatment strategies (NCD)	Not covered	Cover if necessary to determine optimal treatment strategies	Not covered
Surveillance	Not addressed	Not covered	Not covered	Not addressed
Screening	Not covered	Not addressed	Not covered	Not addressed

Summary

- Lymphoma is a heterogeneous group of malignancies with varied treatment dependent on cell histology and stage
- The evidence for this report is based on case series rather than RCTs
- Strength of evidence is low to moderate
- PET is used for a number of indications in the evaluation of lymphoma

Summary: Strength of Evidence

- For KQ1 – diagnostic accuracy, there is a moderate amount of low to moderate strength evidence
- For KQ2 – clinical effectiveness, there is very limited, low strength evidence
- For KQ3 – sub-populations and KQ 4 – safety, there is no evidence
- For KQ5 – costs, there is very limited low strength evidence

Summary

PET indication	Overall Evidence	Strength of Evidence	Guidelines Recommendation	Insurance Coverage
Screening	None	N/A	Against use	No coverage
Diagnosis	Not beneficial. One study of 8 patients.	Low	Against use	No coverage
Original Staging	<p>For HL and aNHL, PET sensitivity and specificity 88-100% and 90-100%; Sensitivity and specificity for CT 88% and 80%.</p> <p>For iNHL, PET/CT had higher sensitivity (90%) than CT (70%) or PET alone (68%). PET appears to detect additional disease but also miss disease detected by CT.</p>	Moderate	For use	All cover
		Low	For use	

Summary

PET indication	Overall Evidence	Strength of Evidence	Guidelines Recommendation	Insurance Coverage
Re-staging	For HL , PET sensitivity 84% and specificity 90-100%.	Moderate	For use	All cover
	For aNHL , PET sensitivity 72% and specificity 100%.	Moderate		
	For iNHL , no evidence	None		
Estimation of Prognosis	For HL and aNHL , PET sensitivity 81%; specificity 97%; PPV 0%, NPV 63%.	Low	For use	All cover
	For iNHL , PET sensitivity 100%; specificity 88%; PPV 62%; NPV 100%.	Low		
Monitoring of Treatment	For HL and aNHL , PET PPV 15-80%; NPV 90-100%.	Moderate	For use if part of a clinical trial. Not for routine use	No coverage
	For iNHL , no evidence	None		
Surveillance	For HL or aNHL , significant false positive PET scans when used in asymptomatic patients in remission.	Low	Against use	No coverage
	For iNHL , no evidence	None		

Questions?

HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on these questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective¹ as expressed by the following standards.²

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms.³

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

¹ Based on Legislative mandate: See RCW 70.14.100(2).

² The principles and standards are based on USPSTF Principles at: <http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm>

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Using Evidence as the basis for a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. *Availability of Evidence:*

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. *Sufficiency of the Evidence:*

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence⁴ using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- the amount of evidence (sparse to many number of evidence or events or individuals studied);
- consistency of evidence (results vary or largely similar);
- recency (timeliness of information);
- directness of evidence (link between technology and outcome);
- relevance of evidence (applicability to agency program and clients);
- bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. *Factors for Consideration - Importance*

At the end of discussion at vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- risk of event occurring;
- the degree of harm associated with risk;
- the number of risks; the burden of the condition;
- burden untreated or treated with alternatives;
- the importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- the degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- value variation based on patient preference.

⁴ Based on GRADE recommendation: <http://www.gradeworkinggroup.org/FAQ/index.htm>

Medicare Coverage and Guidelines

Organization	Date	Outcome	Evidence Base	Grade / Rating
<p>CMS National Policy Decisions – WA HTA</p> <p>Centers for Medicare and Medicaid Services</p> <p>Page: 39</p>	2010	<ul style="list-style-type: none"> ▪ The Centers for Medicare and Medicaid Services have no published National coverage determinations (NCD) for PET scanning in malignancies. <p>This leaves ultimate coverage decisions on FDG PET to local Medicare carriers. In the Decision Memo, CMS (2010) created a two-part framework for analysis of PET use in malignancies – initial treatment strategy and subsequent anti-tumor strategy.</p> <ol style="list-style-type: none"> 1. For Initial Treatment Strategy, CMS will “nationally” cover lymphoma and other solid malignancies for one FDG PET study for determining the optimal location to perform an invasive biopsy and to determine stage of tumor. Moreover, CMS allows local Medicare contractors to make local decisions for coverage of additional PET scans for therapeutic purposes related to initial treatment strategy. 2. For Subsequent Anti-Tumor Treatment Strategy, lymphoma is considered separately from other malignancies. Positron emission tomography is covered without exception. 	<p>Medicare National Coverage Determination (NCD) for positron emission tomography (FDG) for oncologic conditions</p> <p>Manual Section Number: 220.6.17</p>	N/A
<p>Guidelines – WA HTA Page: 38 & 70</p> <p><i>National Comprehensive Cancer Network (NCCN)</i></p> <p><i>Hodgkin Lymphoma</i></p>	2011	<ol style="list-style-type: none"> 1. PET recommended for initial staging of HL and for evaluation of residual masses after treatment 2. PET recommended after completion of treatment to determine prognosis. Use of PET has eliminated the “unproven complete remission” category. 3. PET scans not recommended for routine surveillance. 	Literature Review and Expert Consensus	Fair Quality
<p>Guidelines – WA HTA Page: 70</p> <p><i>National Comprehensive Cancer Network (NCCN)</i></p> <p><i>Non-Hodgkin Lymphoma</i></p>	2011	<ol style="list-style-type: none"> 1. PET scanning is recommended for aNHL for staging of aNHL but is considered optional for other NHLs. 2. NHLs are mostly avid for FDG except for extra-nodal Mantle cell lymphomas. 3. In iNHL, PET <u>not</u> usually performed for staging. In iNHL which appears to be localized a PET scan may help identify occult sites of disease or be useful if concern exists about histologic transformation. 	Literature Review and Expert Consensus	Fair Quality

Organization	Date	Outcome	Evidence Base	Grade / Rating
<p>Guidelines – WA HTA Page: 70</p> <p><i>American College of Radiology (ACR)</i></p> <p><i>Follow-up of Hodgkin Lymphoma</i></p>	2010	Regular follow-up with PET scans in PET-negative patients at the end of therapy is not indicated. However, in patients with clinical findings suspicious for relapse, PET scan may be of value.	Literature Review and Expert Consensus	Fair Quality
<p>Guidelines – WA HTA Page: 70</p> <p><i>American College of Radiology (ACR)</i></p> <p><i>Hodgkin Lymphoma: Favorable prognosis stage I-II</i></p>	2011	Trials will further clarify whether PET response can be used to guide treatment for Hodgkin’s lymphoma. However, changes in therapy (either changing chemotherapy or omitting RT) based on PET response for early-stage patients are not supported by currently available data and should only be performed as part of a clinical trial.	Literature Review and Expert Consensus	Fair Quality
<p>Guidelines – WA HTA Page: 70</p> <p><i>International Harmonization Project in Lymphoma</i></p> <p><i>Recommendations apply to HL</i></p>	2007	<ol style="list-style-type: none"> 1. PET is recommended for assessment of response to primary or salvage treatment. 2. Pet is not required prior to treatment but its performance then improves interpretation of post-treatment PET scans. 3. After-treatment Pet should not be performed before 3 weeks after chemotherapy and 8-12 weeks after radiation therapy. 4. PET during treatment of HL and aNHL is justified if findings will alter management. 	Expert Consensus	Poor Quality

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

PET for Lymphoma	
Safety Outcomes	Safety Evidence
Mortality	
Morbidity	
Radiation Dose Levels	
Incidental Findings	
Contrast Reactions	
Other Adverse Events	
Efficacy – Effectiveness Outcomes	Efficacy / Effectiveness Evidence
PET scan accuracy <ul style="list-style-type: none"> ▪ Sensitivity ▪ Specificity 	
Effect of Pet on the reduction of other tests	
PET for screening patients for Lymphoma	
Use of PET in making a diagnosis / indication	
Diagnostic efficacy to predict relapse or recurrence	
Original staging compared with conventional staging	
Changes in management from PET	
Patient Survival	
Quality of Life	
Patient Satisfaction	
Other Patient Outcomes	
Special Population / Considerations Outcomes	Special Population Evidence

Sex	
Age	
Provider Characteristics	
Patient Selection	
Payer or Beneficiary Type	
Cost	Cost Evidence
Cost Implications	
Direct and indirect <ul style="list-style-type: none"> - Short terms - Over expected duration of use 	
Repeat Procedures	
Cost Effectiveness	

Clinical Committee Evidence Votes

First voting question

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective				
Safe				
Cost-effective				

Discussion

Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second vote

Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____ Not Covered. _____ Covered Unconditionally. _____ Covered Under Certain Conditions.

Discussion Item

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Clinical Committee Findings and Decisions

Next Step: Cover or No Cover

If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions

If covered with conditions, the Committee will continue discussion.

- 1) Does the committee have enough information to identify conditions or criteria?
 - Refer to evidence identification document and discussion.
 - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
 - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.
- 2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
 - What are the known conditions/criteria and evidence state
 - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Efficacy Considerations:

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
 - Direct outcome or surrogate measure
 - Short term or long term effect
 - Magnitude of effect
 - Impact on pain, functional restoration, quality of life
 - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy
 - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
 - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
 - Adverse effect on health that can result in lasting harm or can be life-threatening.
- Other morbidity concerns
- Short term or direct complication versus long term complications
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?