Pediatric Brain Tumor Consortium Neuroimaging Center

Manual of Operations

Boston Children's Hospital

Pediatric Brain Tumor Consortium

Neuroimaging Center

Manual of Operations

Created and Edited by

Tina Young Poussaint, MD
Children's Hospital, Boston

Robert Mulkern, PhD
Children's Hospital, Boston

Fred Fahey, DSc
Children's Hospital, Boston

Voula Osganian, MD, ScD
Children's Hospital, Boston

This grant is supported by funds from the National Cancer Institute (NIH-NCI U01 CA 81456-12)

First produced: 6/1/03. Revised: 1/22/04, 4/23/04, 5/11/04, 5/27/04, 7/6/04, 8/10/04, 11/03/04, 12/21/04, 02/01/05, 05/05/05, 10/19/05, 02/01/06, 05/17/06, 9/26/06, 02/19/07, 01/01/08, 09/03/08, 10/29/08, 11/10/08, 12/02/08, 04/14/09, 07/07/09, 08/19/09, 11/19/09 01/15/10, 02/02/10, 05/10/10, 06/16/10, 06/22/10, 07/27/10, 06/28/11, 09/07/11, 10/11/11, 03/14/12, 04/13/12, 05/04/12, 05/15/12, 10/30/12, 12/18/12, 03/26/13, 05/15/13, 08/15/13, 01/24/14, 4/11/14, 12/15/14, 2/19/15, 9/25/15

TABLE OF CONTENTS

FIGURE, TABLE AND FORM LEGENDS

FIGURE LEGEND

Figure 1	PBTC Organization
Figure 2	PBTC Neuroimaging Center Organization

TABLE LEGEND

Table 1	PBTC Neuroimaging Committee
Table 2	PBTC MR Equipment List
Table 3	PBTC PET Protocol Equipment and Investigators Section A, B, C, D
Table 4	PBTC Institutions and Principal Investigators
Table 5	PBTC Site CRA list
Table 6	PBTC MR Technologists Contact List
Table 7	PBTC Protocols: Neuroimaging Objectives
Table 8	PBTC Protocols: Imaging Components

FORMS LEGEND [Legacy and current forms in use]

Form 100a	MRI Brain Data
Form 100b	MRI Brain Data
Form 2	MRI Quality Assurance
Form 3	Retired: No longer in use
Form 4	PET Brain Data
Form 5	PET Quality Assurance
Form 6	MRI Spine Data
Form 7	Retired: No longer in use
Form 8	Retired: No longer in use
Form 9a	MRI Brain Leptomeningeal Data
Form 10	Retired: No longer in use
Form 11	CT Hemorrhage Data
Form 12	Retired: No longer in use
Form 13	Retired: No longer in use
Form 14	PET Support Data
Form 15	PET Phantom Acquisition Form
Form 16	Merged: Now part of Form 1a
Form 17	Fusion Volumetrics
Form 18	MRI Brain Permeability
Form 19	Site Visit Mandatory Reporting Form
Form 20	^{68}Ge ACR Phantom Acquisition Form
Form 21	Spinal Tumor Volume
Form 22	Comments Form
Form 23	RECIST Measurements
Form 24	MacDonald Criteria

FORMS LEGEND [Legacy and current forms in use] Continued

Form 25	Diffusion Tensor Imaging
Form 26	MR Contrast Survey
Form 27	ADC Histogram Analysis
Form 28	MRI Brain Permeability

Section I
PBTC NIC Manual of Operations
Overview and Goals

I. Overview and Goals

The Pediatric Brain Tumor Consortium (PBTC) is a multidisciplinary cooperative research organization devoted to the study of correlative tumor biology and new therapies for primary CNS tumors of childhood. Its mission is to contribute rapidly and effectively to the understanding and cure of these tumors through the conduct of multi-center, multidisciplinary, innovative studies with designs and analyses based on uniformly high quality statistical science. While the primary mission of the PBTC is to identify through laboratory and clinical science superior treatment strategies for children with brain cancers, the PBTC investigators recognize their profound responsibility to meet the special needs of the children and families as they face this enormous challenge. Members are committed to working within their institutions and communities to improve support services and follow up care for these patients and their families.

The goals of the PBTC Neuroimaging Center (NIC) are:

- To provide leadership in the diagnostic imaging component of all clinical PBTC protocols including the development, implementation and / or coordination of all current and future research protocols for diagnostic imaging studies. These include but are not limited to MRI, MR diffusion, MR perfusion, MR spectroscopy, CT and PET;

- To direct quality assurance activities for the neuroimaging studies including the oversight of compliance with imaging protocols and assessments of diagnostic image quality, data integrity and storage/retrieval;

- To provide centralized review and interpretation of all diagnostic neuroimaging studies and analyze CT, MRI, MRS, PET and other images to generate summary data that will be provided to the Operations and Biostatistics Center (OBC) for statistical analysis;

- To develop a correlative imaging research plan related to the novel therapeutic interventions of the PBTC;

- To ensure PBTC's ability to incorporate imaging endpoints in its overall research program;

- To oversee cross-platform translations for comparative analyses of MRI, MRS, and PET studies.

Section II
PBTC NIC Manual of Operations
Organization

Table 1a: PBTC NIC MR Equipment List

II. Organization

The overall organization of the Pediatric Brain Tumor Consortium (PBTC) is outlined in Figure 1. The consortium includes 10 participating Institutions and a special member (Neurooncology Branch NCI/NINDS), for the recruitment of patients into PBTC protocols, an Operation and Biostatistics Center, a Neuroimaging Center, and Central Laboratories. The Steering Committee is the primary decision-making body for the study with scientific oversight provided by an external Scientific Advisory Board. The work of the Consortium is accomplished through several ad-hoc and standing committees. Specifically, the Neuroimaging Committee (NC) is composed of one neuroradiologist from each participating institution and the PI of the NIC, Dr. Tina Young Poussaint. In addition there are external and internal liaisons on the committee. Under the leadership of Dr. Poussaint, the NC is responsible by consensus for the development of clear and standard procedures for the performance of all PBTC MR Neuroimaging studies across the sites and for all MR neuroimaging quality control procedures. In addition, the NC reviews imaging study data quality reports on a regular basis, provides recommendations regarding possible neuroimaging research questions that may be appropriate to be considered in relevant treatment protocols; and assists in the evaluation of research neuroimaging protocol feasibility, methods, and scientific merit. A PET investigator committee consisting of one PET investigator per site, provides input regarding PET QA, PET analyses, protocols, radiopharmaceuticals and PET research projects.

Figure 1 presents the PBTC organizational structure. Table 1 presents the MR Contacts. Figure 2 presents the organizational structure of the NIC. Figure 3 presents the organizational structure of the Clinical Research Center at Boston Children's Hospital. Table 2 lists the MR Equipment information for each site. Table 3 lists the PET Equipment and Investigators from each site. Table 4 lists the PIs at each respective site. Table 5 lists the CRAs at each site. Table 6 lists the contact MR Technologists at each site.

Figure 1. Pediatric Brain Tumor Consortium Organization

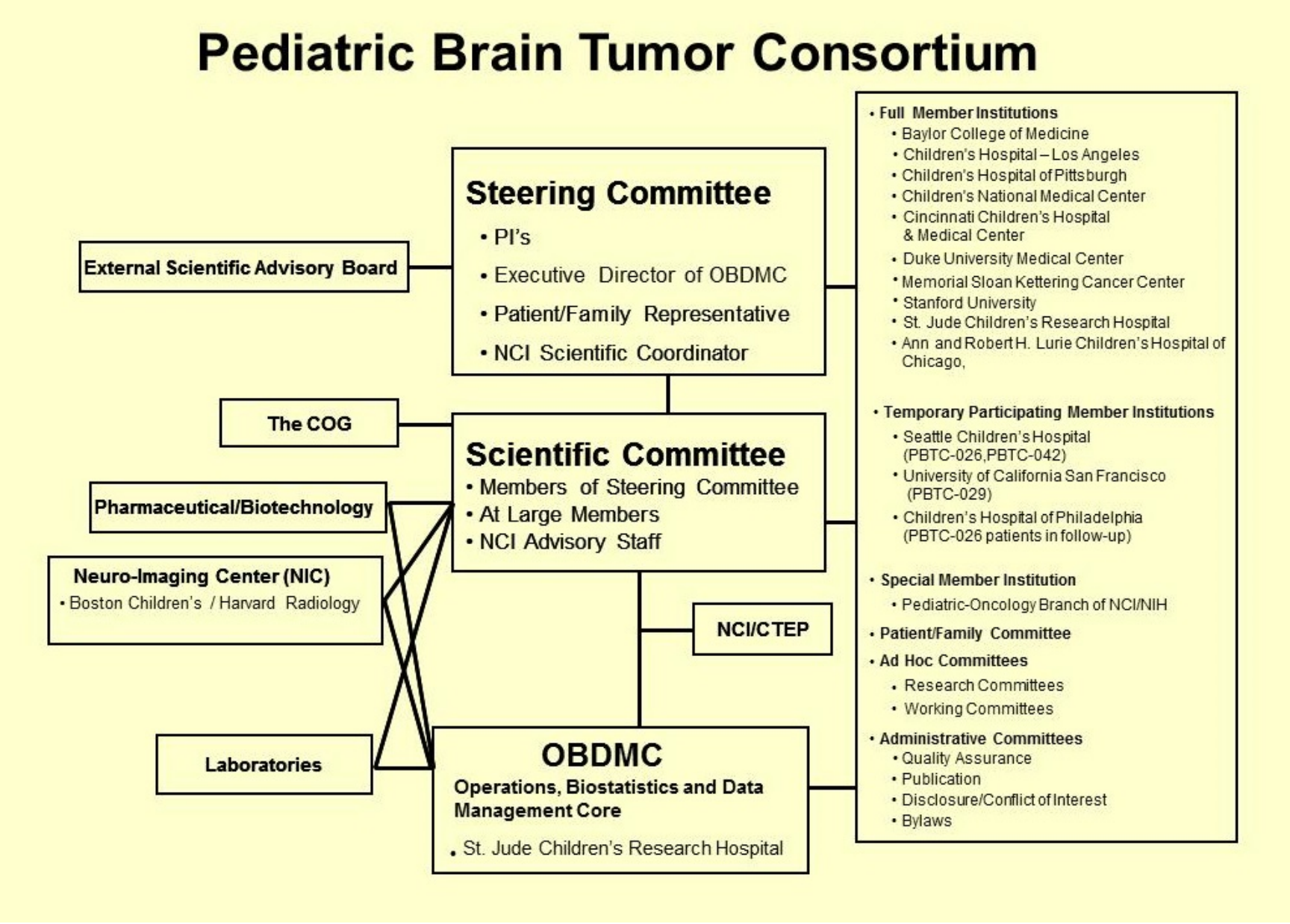


Table 1: PBTC NIC MR Equipment List

Site Code	Institution	Contact Name	Personnel	Contact Telephone	Contact Email
11	Children's National Medical Center Washington, DC	Vezina, Gilbert, MD Holder, Anne	MR Physician MR Technologist	202-476-2389 202-884-2969	gvezina@cnmc.org aholder@cnmc.org
13	Duke University Medical Center Durham, NC	Lascola, Christopher, MD Hinton, Joseph	MR Physician MR Technologist	919-684-7218 919-684-7254	christopher.lascola@duke.edu joseph.hinton@duke.edu
14	Boston Children's Hospital Boston, MA	Mulkern, Robert, PhD Biagiotti, Diane	MR Physicist MR Technologist	617-355-3737 617-355-5154	robert.mulkern@childrens.harvard.edu diane.allen@childrens.harvard.edu
15	Children's Hospital Pittsburgh of UPMC Pittsburgh, PA	Panigrahy, Ashok, MD Willaman, Dennis	MR Physician MR Technologist	412-692-5510 412-693-3038	ashok.panigrahy@chp.edu dennis.willaman@chp.edu
16	St Jude Children's Research Hospital Memphis, TN	Patay, Zoltan, MD Jones, Kendri Brady, Samuel	MR Physician MR Technologist MR Technologist (QA)	901-595-2718 901-595-2013 901-595-8728	zoltan.patay@stjude.org kendri.jones@stjude.org samuel.brady@stjusde.org
18	Texas Children's Hospital at Baylor Houston, TX	Jones, Jeremy, MD Dowdy, Dionne	MR Physician MR Technologist	832-822-5234 832-824-6330	jyjones@texaschildrens.org drdowdy@texaschildrens.org
20	National Institutes of Health Bethesda, MD	Patronas, Nicholas, MD Evers, Robert	MR Physician MR Technologist	301-402-5726 301-402-5586	npatronas@cc.nih.gov robert.evers@nih.gov
21	Lurie Children's Hospital of Chicago Chicago, IL	Paige Nelson	Research Coordinator	312-227-3479	pnelson@luriechildrens.org
22	Cincinnati Children's Hospital Medical Center Cincinnati, OH	Jones, Blaise, MD Young, Julie	MR Physician MR Technologist	513-636-7475 513-636-5805	blaise.jones@cchmc.org julie.young@cchmc.org
23	Children's Hospital Los Angeles Los Angeles, CA	Nelson, Marvin, MD Kohatsu, Arthur	MR Physician MR Technologist	323-361-2411 323-361-2411	mdnelson@chla.usc.edu akohatsu@chla.usc.edu
24	Memorial Sloan-Kettering Cancer Center New York, NY	Haque, Sofia, MD Mair, Thomas	MR Physician MR Technologist	212-639-7170 212-639-6342	haques@mskcc.org mairt@mskcc.org
25	Lucile Packard Children's Hospital at Stanford Palo Alto, CA	Yeom, Kristen, MD White, Allan	MR Physician MR Technologist	650-721-2388 650-497-8376	kyeom@stanford.edu awhite@lpch.org

Table 1a: PBTC NIC MR Equipment List

Site Code	Institution	Equipment Vendor/Model*	Software Version	Contrast
11	Children's National Medical Center Washington, DC	GE Discovery 450 (1.5T) GE Optima 450W (1.5T) GE Discovery 750 (3.0T)	24X 24X 24X	Gadavist 0.1 ml/Kg Dotarem 0.2 ml/Kg
13	Duke University Medical Center Durham, NC	Siemens 3T Skyra (2) Siemens 3T TimTrio (1) Siemens 1.5T Aera (2) Siemens 1.5T Avanto (2) GE 1.5T 450w (2) GE 1.5T Signa HDXT (1)	D13 B19 D13 B17 DV25 V15	Not Supplied
14	Boston Children's Hospital Boston, MA	GE 1.5T (1) Siemens 3T (4) Siemens 1.5 (1)	15.0 VB17 VB17	Gadavist 0.1 ml/Kg
15	Children's Hospital Pittsburgh of UPMC Pittsburgh, PA	GE 1.5T (2) GE 3.0T (1) Siemens Skyra (1)	16.0 16.0 Not available.	Magnevist 0.2 ml/Kg Multihance 0.2 ml/Kg
16	St Jude Children's Research Hospital Memphis, TN	Siemens Avanto Fit - 1.5T Siemens Prisma (2) 3.0T Siemens Skyra (1) 3.0T	Avanto Fit – Syngo MR A13B Prisma (x2)-Syngo MR D13D Skyra-E11	Magnevist 0.1 ml/kg
18	Texas Children's Hospital at Baylor Houston, TX	Philips Achieva (1.5T) (4) Philips Achieva (3.0T)	Manufacturer supplied software	Gadavist 0.1 ml/Kg Dotarem 0.2 ml/Kg
20	National Institutes of Health Bethesda, MD	Siemens VERIO 3.0T Philips Tx Achieva 3.0 T Siemens mMR 3.0 T Philips 1.5T Achieva Siemens Aera 1.5 T	VB17 3.2.2.0 3.2.3.1 vb20 3.2.3.2 VD13	Magnavist 0.2 ml/Kg Multihance 0.2 ml?kg Prohance 0.2 ml/Kg Gadavist 0.1 ml/Kg
21	Lurie Children's Hospital of Chicago Chicago, IL	Siemens Aera (2) 1.5T Siemens Skyra (1) 3T GE Signa HDxt(2) 1.5T	Syngo MR D13 Numaris/4 Syngo MR D13 Numaris/4 1.5T Version 23	Multihance 0.2 ml/Kg
22	Cincinnati Children's Hospital Medical Center Cincinnati, OH	GE 1.5T (4 nos) Philips 3T (1) Siemens 1.5T (1) GE 3T (1) Philips 1.5T (2)	s/w ver. 23 s/w ver. 5.1 s/w ver. VB17 s/w ver. 24 s/w ver. 5.1	Dotarem 0.2 ml/Kg
23	Children's Hospital Los Angeles Los Angeles, CA	GE (1.5T) Philips (1.5T) Philips (3.0T)	Signa – 9.1 M4 Achieva 3.0 Achieva 3.0	Gadavist 0.1 ml/Kg
24	Memorial Sloan-Kettering Cancer Center New York, NY	GE Signa** 750W GE Signa*** 1.5T GE 450W 450W GE 750 3T	GE Signa 750W DV25 GE Signa 1.5T V12 GE 450W DV24 GE 750 3T DV24	Gadavist 0.1 ml/Kg
25	Lucile Packard Children's Hospital at Stanford Palo Alto, CA	MR1 450W 1.5 T MR2 750 3T MR3 750 3T	DV23_VO1 DV25_RO1 DV25_RO1 Modular building MRI	Multihance 0.2 ml/Kg Gadavist 0.1 ml/Kg

*Note that Equipment Vendor/Model column lists field strength (1.5T or 3.0T) and number of magnets if multiple present at site.
** Will be replacing GE Signa 3T (in the next 1.5-2.5 years)
*** Will be removed once construction is complete (in the next 1.5-2.5 years)

Table 2: PBTC NIC PET Equipment List

SECTION A: Equipment

Site Code	Institution	Equipment Vendor/Model	Contact Name	Personnel	Contact Telephone	Contact Email
11	Children's National Medical Center Washington, DC	GE Discovery 690 PET/MDCT	Pranav Vyas, MD Sarah McKenney	PET Physician PET Physicist	202-476-5630 202-476-5075	pvyas@childrensnational.org smckenney@childrensnational.org
13	Duke University Medical Center Durham, NC	GE Discovery 690 PET/CT GE Discovery IQ 5-ring PET/CT	James, Olga, MD Turkington, Timothy PhD Hawk, Thomas, BS	PET Physician PET Physicist Computer Specialist	919-684-7647 919-684-7706 919-684-7714	olga.james@dm.duke.edu timothy.turkington@duke.edu thomas.hawk@duke.edu
14	Boston Children's Hospital Boston, MA	Siemens mCT 40 PET/CT	Treves, Ted, MD Voss, Stephan, MD Fahey, Fred, DSc Cao, Xinhua, PhD	PET Physician PET Physician PET Physicist Computer Specialist	617-355-7935 617-355-8317 617-355-2809 617-355-5563	ted.treves@childrens.harvard.edu Stephan.voss@childrens.harvard.edu Frederic.fahey@childrens.harvard.edu xinhua.cao@childrens.harvard.edu
15	Children's Hospital Pittsburgh of UPMC Pittsburgh, PA	GE Discovery DVCT PET/CT	Joyce, Judith, MD N/A Czachowski, Michael, MBA	PET Physician PET Physicist Nuclear Tech Supervisor	412-647-0104 412-692-9518	joycejm@upmc.edu Michael.Czachowski@chp.edu
16	St Jude Children's Research Hospital Memphis, TN	GE Discovery 690	Shulkin, Barry, MD, MBA Brady, Samuel, PhD Foster, Nancy	PET Physician PET Physicist Computer Specialist	901-595-3347	Barry.shulkin@stjude.org Samuel.brady@stjude.org Nancy.foster@stjude.org
18	Texas Children's Hospital at Baylor Houston, TX	Philips 3T PET/MRI TF Philips Gemini TF Select 16 Slice PET/CT	Orth, Robert, MD, PhD McMullen, Tara Walters, Veronica	PET Physician PET Technologist Admin. Asst.	832-822-1239 832-826-8578 832-826-8525	rcorth@texaschildrens.org tlmcmull@texaschildrens.org vswalter@texaschildrens.org
20	National Institutes of Health Bethesda, MD	GE Advance PET HRRT Siemens MCT PET/CT	Herscovitch, Peter, MD Barker, Craig, PhD Fraser, Charles	PET Physician PET Physicist Computer Specialist	301-451-4248 301-451-3558 301-451-3591	pherscovitch@cc.nih.gov cbarker@cc.nih.gov cfraser@cc.nih.gov
21	Lurie Children's Hospital of Chicago Chicago, IL	GE PET/CT Discovery 690 12123PT6	Shore, Richard, MD Delilah Burrowes, MD Christina Sammet, PhD	PET Physician PET Physician PET Physicist	312-227-3504 312-227-4388 312-227-3393	rshore@luriechildrens.org dburrowes@luriechildrens.org csammet@luriechildrens.org
22	Cincinnati Children's Hospital Medical Center Cincinnati, OH	Philips Ingenuity TF	Michael J. Gelfand, MD Susan E. Sharp, MD (backup) Lisa Lemen, PhD Jay Moskovitz (information tech) Leonid Rozhkov (analytic	PET Physician PET Physician PET Physicist Computer Specialist Computer Specialist	513-636-7650 513-636-6662 513-558-2197 513-636-5981 513-803-0545	Michael.gelfand@cchmc.org Susan.sharp@cchmc.org Lisa.lemen@uc.edu Jay.moskovitz@cchmc.org Leonid.rozhkov@cchmc.org
23	Children's Hospital Los Angeles Los Angeles, CA	Philips/Gemini GXL16 PET/CT	Hollie A. Lai, MD	PET Physician	323-361-4570	hlai@chla.usc.edu
24	Memorial Sloan-Kettering Cancer Center New York, NY	General Electric PET/CT	Neeta Pandit-Taskar, MD Ross Schmidtlein Brad Beattie John Humm Hovanes Kalaigian	PET Physician PET Physicist PET Physicist PET Physicist Computer Specialist	212-639-7372 212-639-8082 646-888-2579 212-639-7367 212-639-7382	Pandit-n@mskcc.org schmidtr@mskcc.org beattieb@mskcc.org hummj@mskcc.org kalaigih@mskcc.org
25	Lucile Packard Children's Hospital at Stanford Palo Alto, CA	GE D690 PET/CT GE D600 PET/CT	Andrew Quon, MD Shawna Kinsella, CNMT	PET Physician PET Technologist	650-725-4711 650-725-8263	aquon@stanford.edu skinsella@stanfordhealthcare.org

Table 2: PBTC NIC PET Equipment List

SECTION B Radiopharmaceuticals **SECTION C Image Analysis Equipment** **SECTION D Research Interests**

Site Code	Institution	Radiopharmaceuticals Used with Brain imaging	Image Analysis Equipment	Brain Imaging research at site unrelated to the PBTC
11	Children's National Washington, DC	FDG	GE AW workstation	Projects in fetal MRI, fMRI
13	Duke University Medical Center Durham, NC	F18-FDG,F18-FLT, F18-fluorbetapir	GE AW MIMVista Linux WS	Radiolabeled mab therapy for brain tumors - PET f/u, Metabolic effects of radiation therapy on cognitive function (FDG), dementia, plaque imaging compounds for dementia , FLT
14	Boston Children's Hospital Boston, MA	FDG, FLT	Hermes Medical Solution Workstation	Animal Micro PET, Epilepsy-spect
	Dana Farber Cancer Institute Boston, MA	FDG, FLT (pending)	ECAT Software (CTI), Xeleris/AW (GE), Hermes, Siemens Leonardo/True D	Adult brain tumors. Central PET core lab for global multi-center trial of lapatinib in brain metastases in women with breast cancer
15	Children's Hospital Pittsburgh of UPMC Pittsburgh, PA	FDG	GE Discovery DVCT	Possible FLT in near future
16	St Jude Children's Research Hospital Memphis, TN	11 C-MET-PET 18 F-FDG	Hermes Medical Solution Workstation	C-11 methionine uptake for CNS tumor survey Relation of histology to FDG uptake
18	Texas Children's Hospital at Baylor Houston, TX	FDG	MIM vista software Philips Portal	No participation in Brain imaging research prior to PBTC
20	National Institutes of Health Bethesda, MD	FDG, H20, fdopa, fcway, flumazenil, nnc, leucine, dasb, fallypride, raclopride, methylreboxitine, DTBZ, FP-TZTP, FCWAY, arachidonic acid, docosahexaenoic acid, acetate Ga-68 DOTATATE	PACS	epilepsy, Alzheimer's, Parkinson's, schizophrenia, depression, obsessive compulsive disorder, tumor, alcohol abuse, movement disorders, Fragile X, TBI
21	Lurie Children's Hospital of Chicago Chicago, IL	FDG	GE PET/CT Discovery 690 12123PT6 AW	N/A
22	Cincinnati Children's Hospital Medical Center Cincinnati, OH	F-18-FDG (2,3), Tc-99m-ECD (2,3), Tc-99m-HMPAO (2,3), F-18-fallypride (1,3,4), F-18-FDOPA (1,2,3), F-18-choline (1,3,5), C-11-methionine (1,2,6) * * (1)=Available in co-operation with Kettering Medical Center, Dayton, OH. (2)=Used for clinical studies. (3)=Available locally. (4)=Used for human research studies only. (5)=Only used for non-human experiments to date. (6)=Will require patient transportation to off campus site.	Analyze 10, SPM, Brain Lab	Epileptogenic focus localization, Dopamine transporter density (1)
23	Children's Hospital Los Angeles Los Angeles, CA	F18-FDG	N/A	N/A
24	Memorial Sloan-Kettering Cancer Center New York, NY	FDG, FLT, and FACB	GE PET VCAR Hermes Medical Systems	F-choline in brain (PI at site is Kathryn Beall)
25	Lucile Packard Children's Hospital at Stanford Palo Alto, CA	FDG, FLT, Amyvid	GE Advantage Windows	Amyvid (AV-45)

Table 3. PBTC Institutions and Principal Investigators

CHILDREN'S NATIONAL MEDICAL CENTER	CHILDREN'S HOSPITAL OF PHILADELPHIA
Roger Packer, M.D. **Children's National Medical Center** Department of Neurology 111 Michigan Avenue, NW Washington, DC 20010 TEL: 202/884-2120 FAX: 202/884-5226 E-MAIL: rpacker@cnmc.org SITE 11	**Peter Phillips, M.D.** **The Children's Hospital of Philadelphia** Division of Neuro-Oncology 4th Floor Wood Building 3400 Civic Center Boulevard Philadelphia, Pennsylvania 19104 TEL: 215/590-2800 FAX: 215/590-3709 E-MAIL: phillipsp@email.chop.edu SITE 12
BRAIN TUMOR CENTER AT DUKE	**DANA-FARBER CANCER INSTITUTE**
Sri Gururangan, M.D. **The Brain Tumor Center at Duke** Duke University Medical Center Box 3624 Durham, North Carolina 27710 TEL: 919/668-6288 FAX: 919/681-1697 E-MAIL: gurur002@mc.duke.edu SITE 13	**Mark W. Kieran, M.D., Ph.D.** **Dana-Farber Cancer Institute** Department of Pediatrics 44 Binney Street Boston, Massachusetts 02115 TEL: 617/632-4907 FAX: 617/632-4248 E-MAIL: mark_kieran@dfci.harvard.edu SITE 14
ST. JUDE CHILDREN'S RESEARCH HOSPITAL	
James M. Boyett, Ph.D. **Executive Director, PBTC Operations & Biostatistics Center** St. Jude Children's Research Hospital Department of Biostatistics Memphis, TN 38105 TEL: 901/595-4986 FAX: 901/595-4184 EMAIL: james.boyett@stjude.org Site 16	**Larry Kun, M.D.** **St. Jude Children's Research Hospital** Department of Radiation Oncology 262 Danny Thomas Place Memphis, Tennessee 38105-3678 TEL: 901/595-3604 FAX: 901/595-3113 E-MAIL: larry.kun@stjude.org SITE 16
CHILDREN'S HOSPITAL OF PITTSBURGH	**CHILDREN'S HOSPITAL & REGIONAL MEDICAL CENTER – SEATTLE**
Ian Pollack, M.D. **Children's Hospital of Pittsburgh** Department of Neurological Surgery 3705 Fifth Avenue Pittsburgh, Pennsylvania 15213 TEL: 412/692-5090 FAX: 412/692-5921 E-MAIL: ian.pollack@chp.edu SITE 15	**J. Russell Geyer, M.D.** **Seattle Children's Hospital** Department of Pediatrics 4800 Sand Point Way NE B6553 Seattle, Washington 98105 TEL: 206/987-6664 FAX: 206/987-3946 E-MAIL:russ.geyer@seattlechildrens.org SITE 17

TEXAS CHILDREN'S CANCER CENTER / BAYLOR	UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
Murali Chintagumpala, M.D. & Patricia Baxter, M.D. **Texas Children's Cancer Center** 6621 Fannin Street, MC 3-3320 Houston, Texas 77030 TEL: 800/CANCER9 FAX: 832/825-4299 E-MAIL: mxchinta@txccc.org; pabaxter@txch.org SITE 18	**Michael Prados, M.D.** **University of California, San Francisco** Department of Neurological Surgery 400 Parnassus, Room A808 San Francisco, California 94143-0372 TEL: 415/353-2966 FAX: 415/353-2167 E-MAIL: pradosm@neurosurg.ucsf.edu SITE 19

Table 3. PBTC Institutions and Principal Investigators (continued)

NATIONAL INSTITUTES OF HEALTH	CHILDREN'S MEMORIAL HOSPITAL
Kathy Warren, M.D. **NIH/NCI** Pediatric Oncology Branch Bldg 10, CRC, Rm 1-5750 Bethesda, MD 20892-1104 TEL: 301/435-4683 FAX: 301/451-7052 E-MAIL: warrenk@mail.nih.gov SITE 20	**Stewart Goldman, M.D.** **Children's Memorial Hospital** 2300 Children's Plaza Chicago, IL 60614-3394 TEL: 773/ 880-4562 FAX: 773/880-3223 E-MAIL: sgoldman@northwestern.edu SITE 21
CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER	**CHILDREN'S HOSPITAL LOS ANGELES**
Maryam Fouladi, M.D. **CCHMC** Medical Director, Neuro-Oncology Program 3333 Burnet Avenue Cincinnati, OH 45229-3062 TEL: 513/636-4266 FAX: 513/636-3549 E-MAIL: maryam.fouladi@cchmc.org SITE 22	**Girish Dhall, M.D.** **CHLA** Neural Tumors Program 4650 Sunset Boulevard, MS #54 Los Angeles, CA 90027-6016 TEL: 323/361-4629 FAX: 323/361-8165 E-MAIL: gdhall@chla.usc.edu SITE 23
MEMORIAL SLOAN-KETTERING CANCER CENTER	**LUCILE PACKARD CHILDREN'S HOSPITAL AT STANFORD**
Ira Dunkel, M.D. **MSKCC** Pediatric Oncology Branch 1275 York Avenue New York, NY 10065 TEL: 212/639-2153 FAX: 212/717-3239 E-MAIL: dunkeli@mskcc.org SITE 24	**Paul Graham Fisher, M.D.** **Stanford** Neurology and Pediatrics 750 Welch Road, Suite 317 Palo Alto, CA 94304-1510 TEL: 650/721-5889 FAX: 650/723-7299 E-MAIL: pfisher@stanford.edu SITE 25

Table 4. PBTC Clinical Research Associates/Nurses

Primary Contact	Institution/ Site ID	Office Phone	Email Address	Role	Mailings
Emily Sparks	CCHMC (Cincinnati) OH076	513-636-7810	Emily.sparks@cchmc.org	CRA	All
Sharon DiBridge	Children's Pittsburgh PA010	412-692-7070	sharon.dibridge@chp.edu	CRA	All
Sabrina Malik	Children's National DC008	202-476-5115	samalik@childrensnational.org	CRA	All
Kelley Haley	CHLA (Los Angeles) CA009	323-361-2480	khaley@chla.usc.edu	CRA	All
Charlene Flahiff	Duke NC010	919-613-4527	Charlene.flahiff@duke.edu	CRA	All
Emily Golbeck	Lurie Children's IL045	312-227-4858	EGolbeck@luriechildrens.org	CRA	All
Kathryn Ward	MSKCC NY016	646-888-5723	wardk@mskcc.org	CRA	All
Sonja Crandon	NIH-POB MD004	301-496-8809	sonja.crandon@nih.gov	CRA	All
Leah White	Stanford CA139	650-725-4708	Lwhite15@stanford.edu	CRA	All
Dillon Robinson	St. Jude TN024	901-595-5922	Dillon.robinson@stjude.org	CRA	All
Susan Burlingame	Texas (Baylor) TX040	832-824-1532	sxburlin@txch.org	CRA	All
Ratnakar Patti	CHOP PA076	267-426-5503	pattir@email.chop.edu	CRC	All
Whitney Stewart	UCSF CA385	415-353-9387	Whitney.Stewart@ucsf.edu	CRA	29B
April Smith	Children's Seattle WA061	206-884-7274	april.smith@seattlechildrens.org	CRA	All
Additional Staff	**Institution**	**Office Phone**	**Email Address**	**Role**	**Mailings**
Lori Backus	CCHMC (Cincinnati)	513-636-2047	lori.backus@cchmc.org	CRA	All
Courtney Blank	CCHMC (Cincinnati)	513-803-3255	courtney.blank@cchmc.org	CRA	Back up only
Renee Doughman	CCHMC (Cincinnati)	513-803-0471	Renee.doughman@cchmc.org	Regulatory	Regulatory – Primary for PBTC
Laurie Grimme	CCHMC (Cincinnati)		laurie.grimme@cchmc.org	CRA	
Julie McDonald	CCHMC (Cincinnati)	513-636-8773	julie.mcdonald@cchmc.org	CRA	
Linda Hinds	CCHMC (Cincinnati)	513-803-9443	linda.hinds@cchmc.org	RN	Nursing Committee
Percy Julian	Children's National	202-476-6551	PJulian@childrensnational.org	CRA	All
Chad Stephans	Children's National	202-476-4481	cstephan@childrensnational.org	CRA	All, primary regulatory
Swapna Pamu	Children's National	202-476-6493	spamu@childrensnational.org	CRA	All
Kaitlyn Hardy	Children's National	202-476-5016	KaHardy@childrensnational.org	CRA	All
Judith Cawley	Children's Pittsburgh	412- 692-5059	judith.cawley2@chp.edu	Regulatory	Regulatory
Angela Connelly (Krol)	Children's Pittsburgh	412-692-8047	angela.krol@chp.edu	Research RN	All
Meg Fromuth	Children's Pittsburgh	412-692-8926	Margaret.fromuth2@chp.edu	CRA	All; part-time but needs to be on all CRA notifications

Table 4: PBTC Clinical Research Associates/Nurses (continued)

Carole Rimer	Children's Pittsburgh	412-692-7336	Carole.rimer@chp.edu	Research Nurse	Covering during Angie's leave
Dalila Ortega	CHLA	323-361-5629	dlopez@chla.usc.edu	Regulatory	All except queries
Jasmine Pauly	CHLA		jpauly@chla.usc.edu	CRC	All
Waynette Freeman	Duke	919-684-3440	maria.freeman@duke.edu	Regulatory	Regulatory
Denise Jaggers	Duke	919-613-6803	denise.jaggers@dm.duke.edu	CRA	Immuno protocols, backup CRA
Elizabeth Miller	Duke	919-681-7478	elizabeth.s.miller@dm.duke.edu	Regulatory	Regulatory
Kirsten Fuller	MSKCC	646-888-5719	fullerk@mskcc.org	Manager	All
Ryan Turner	MSKCC	646-888-5723	TurnerR@mskcc.org	CRA	All
Alicia Lashley	MSKCC	212-639-3162	LashleA1@mskcc.org	CRA Radiology	**N12 only**
Stephanie Vitolano	MSKCC	212-639-3384	vitolans@mskcc.org	Research RN	All except queries
Mary Petriccione	MSKCC	212-639-3384	petriccm@mskcc.org	Research RN	All except queries
Cheryl Fischer	MSKCC	212-639-2153	fischerc@mskcc.org	Research RN	All except queries
Natasha Brunson	NIH-POB	301-451-7747	brunsonn@mail.nih.gov	Data Mgr	Queries
Andy Gillespie	NIH-POB	301-402-1848	gillesan@mail.nih.gov	Research Manager	All
Sharon Mavroukakis	NIH-POB	301-231-4876	mavrouks@mail.nih.gov	Research nurse	
Kelly Bryant	NIH-POB		kelly.bryant@nih.gov	Protocol specialist	Regulatory
Kate Lyons	St. Jude	901-595-5597	Kate.lyons@stjude.org	CRA	Regulatory
Molly Clarke	St. Jude	901-595-3567	molly.clarke@stjude.org	Research RN	All except queries
Johanna Pranica	St. Jude	901-595-5787	Johanna.pranica@stjude.org	CRA	All, Backup CRA
Kelly Booten	St. Jude	901-595-5353	kelley.booten@stjude.org	CRA	All; Backup CRA
Manju George	Texas	832-824-1531	msgeorge@texaschildrens.org	CRA	Backup only
Renee Klenke	Texas	832- 824-4570	raklenke@txch.org	Research RN	All except queries
Susan Milligan	Texas	832-824-2138	sdmillig@txch.org	CRA	All
Suzanne Wheeler (formerly Hegemier)	Texas	832- 824-4217	shwheele@txch.org	Research RN	All except queries
James Yandell	Texas	832-824-6657	jxyandel@texaschildrens.org	Regulatory	Regulatory
Cory Hoeppner	Children's Seattle	206-987-3176	corrine.hoeppner@seattlechildrens.org	NP	All except queries
Jonathan Liaw-Gray	Children's Seattle	206-884-5184	jonathan.liawgray@seattlechildrens.org	CRA	Backup only
Celeste Oglesby	Children's Seattle	206-987-1457	celeste.oglesby@seattlechildrens.org	Research RN	All except queries

Table 5. PET and MR QA Contacts

PET QA	MR QA
CHILDREN'S MEMORIAL HOSPITAL – CHICAGO	
Paige Nelson (PET Contact) 312.227.3479 PNelson@lauriechildrens.org	Paige Nelson (MR Contact) 312.227.3479 PNelson@lauriechildrens.org
BOSTON CHILDREN'S HOSPITAL	
Fred Fahey (PET Contact) 617.355.2809 Frederic.Fahey@childrens.harvard.edu	Robert Mulkern (MR Contact) 617.355.3737 Robert.Mulkern@childrens.harvard.edu
BRAIN TUMOR CENTER AT DUKE	
Timothy Turkington (PET Contact) 919.684.7706 timothy.turkington@duke.edu	Christopher Lascola (MR Contact) 919.684.7218 christopher.lascola@duke.edu
ST. JUDE'S CHILDREN'S RESEARCH HOSPITAL	
Samuel Brady (PET Contact) 901.595.8753 Samuel.brady@stjude.org	Samuel Brady (MR Contact) 901.595.8753 Samuel.brady@stjude.org
CHILDREN'S HOSPITAL OF PITTSBURGH	
Michael Czachowski (PET Contact) 412.692.9518 Michael.Czachowski@Chp.edu	Ashok Panigrahy (MR Contact) 412.692.5510 Ashok.panigrahy@chp.org
TEXAS CHILDREN'S CANCER CENTER / BAYLOR	
Christine Sholar (PET Contact) 832.822.5315 mcsholar@texaschildrens.org	Jeremy Jones (MR Contact) 832.824.5325 jyjones@texaschildrens.org
CHILDREN'S HOSPITAL LOS ANGELES	
Hollie Lai (PET Contact) 323.361.4570 hlai@chla.usc.edu	Marvin Nelson (MR Contact) 323.361.2169 mdnelson@chla.usc.edu
CHILDREN'S NATIONAL MEDICAL CENTER	
Sarah McKenney (PET Contact) 202.476.5075 smckenney@childrensnational.org	Anne Holder (MR Contact) 202-884-2969 aholder@cnmc.org
NATIONAL INSTITUTES OF HEALTH	
Craig Barker (PET Contact) 301.451.3558 cbarker@nih.gov	Nicholas Patronas (MR Contact) 301.402.5726 npatronas@nih.gov
LUCILE PACKARD CHILDREN'S HOSPITAL AT STANFORD	
Andrew Quon (PET Contact) 650.725.4711 aquon@stanford.edu	Allan White (MR Contact) 650-497-8376 awhite@lpch.org
CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER	
Lisa Lemen (PET Contact) 513.558.2197 lemenll@uc.edu	Suraj Serai (MR Contact) 513.636.5595 suraj.serai@ccmc.org

Table 5. PET and MR QA Contacts (Continued)

PET QA	MR QA
MEMORIAL SLOAN-KETTERING CANCER CENTER	
Neeta Pandit-Taskar (PET Contact) 212.639.3046 Pandit-n@mskcc.org	Duane Nicholson (MR Contact) 212.639.5392 Nichold2@mskcc.org

Section III
PBTC NIC Manual of Operations
Neuroimaging Studies

III. Neuroimaging Studies

This section outlines and provides an overview of the different types of neuroimaging studies that are used in various PBTC protocols. The NIC assists in therapeutic protocol development by providing standardized language describing diagnostic qualitative and quantitative neuroimaging procedures and their implementation in participating institutions. Protocols and implementation are developed by consensus and in collaboration with the Neuroimaging and PET Investigator Committees. The detailed procedures for standard sequences, contrast doses and infusion times, image data storage, image data transfer, tumor measurement and response criteria, and volumetric analysis can be found in each specific imaging study protocol in the Appendix. A brief description of each study follows.

A. MRI: Standard Sequences

MRI is the primary neuroimaging modality used for monitoring the effects of the PBTC therapeutic protocols. MRI is sufficiently mature to allow for a standardization of imaging protocols between sites despite disparities between MRI manufacturers. The NIC staff provides each site with a minimum set of MRI sequences, which must be performed for inclusion into the database including T1, T2, FLAIR, gradient sequences and susceptibility weighted sequences. Standardization of all pulse sequence parameters including slice plane selection, slice thickness, in-plane matrices, spatial resolution, repetition times, echo times, and echo train lengths is mandated among the sites.

Data analysis of standard MR images includes tumor location, tumor signal characteristics, and presence of hemorrhage, particularly in antiangiogenesis protocols. Tumor volume is obtained from FLAIR or T2 sequences and T1 gadolinium sequences (enhancing and nonenhancing: cyst/necrosis) using the Vitrea workstation (Vital Images, Plymouth, MN) (See Form 1a). For leptomeningeal disease, tumor location, presence of disease (whether linear or nodular (single or multiple)) is recorded. (See form 6 and 9).

For hemorrhage assessment, presence of hemorrhage is recorded and an estimate of the percentage of hemorrhage in the tumor is determined and categorized as 0-25%, 26-50%, 51-75% and greater than 75%. The signal characteristics of the hemorrhage are determined on the following sequences: T1, T2, FLAIR, and diffusion, perfusion, gradient echo and suscepitiblity weighted series (See Form 1a).

B. CT

Parameters will be established for CT data acquisition for those PBTC protocols requiring CT imaging. Standardization of all parameters will be done. CT scans are done as needed for hemorrhage assessment in the acute setting (See Form 11).

C. MR Spectroscopy

MRS offers a noninvasive in vivo approach to biochemical analysis. MRS provides additional quantitative information regarding cellular metabolites since signal intensity is linearly related to steady-state metabolic concentration. MRS may detect cellular biochemical changes prior to the detection of morphological changes by MRI or other imaging modalities. Some of the more important applications of proton MRS in the assessment of CNS neoplasia at the current time are to evaluate cellular response to

therapy, to direct tissue biopsies, to plan surgical resections, to define disease extent and to differentiate tumor progression from treatment effects such as necrosis.

Single voxel MRS PRESS sequences has been required at all sites which can be substituted by multivoxel technique at sites with this capability. Please note all sites should do a screen save of the MRS spectrum with the ratios displayed on the image. In addition MRS raw data should be saved and transferred to the OBC (See MRS raw data transfer-Section 4C).

Calculation of MRS ratios includes NAA/tCr, choline/tCr, lipid/tCr. Other metabolites of interest include citrate, myoinositol, and taurine.

D. MR Diffusion

Diffusion imaging is standardized using single-shot echoplanar spin echo based diffusion sequences. MR diffusion has been useful in the characterization of tissue, tumor cellularity, tumor grading, tumor response to treatment and distinction of tissue types. Diffusion tensor imaging (DTI) provides visualization of fiber bundle direction and integrity which has applications including presurgical planning or coregistration of tractography data with radiosurgical planning and functional imaging MR data as well as assessing treatment-induced white matter changes.

Standardization of sequence parameters includes slice thicknesses, axial locations, spatial resolution, TE and b-factor values.

For standard MR diffusion, a region of interest is placed over the solid part of the tumor divided by the MR diffusion region of interest in the frontal white matter and the ratio value recorded. Coordination with region-of-interest (ROI) from the CBV map is done as necessary. For DTI, fractional anisotropy (FA), apparent diffusion coefficient (ADC) and RGB-orientation color maps are created using software created for this purpose using IDL (ITT Visual Information Solutions, Boulder, CO). TrackVis is used to visualize and analyze fiber track data from diffusion MR imaging. In selected protocols, ADC histogram and functional diffusion map analyses are done.

E. MR Perfusion

MR perfusion imaging is currently being used to evaluate cerebral perfusion dynamics by analyzing hemodynamic parameters including relative cerebral blood volume, relative cerebral blood flow, and transit time, all as complementary to conventional MR imaging. The MRI perfusion data is analyzed using the method of Ostergaard et al developed at MGH, including maps of rCBV, rCBF, CBV corrected for permeability changes, and a T2-based permeability-surface area product measurement.

An MR perfusion region of interest is placed in the solid part of the tumor with highest CBV and divided by MR perfusion region of interest from the frontal white matter and the ratio value recorded.

Parameters for echoplanar gradient echo mode single-shot perfusion imaging are standardized.

MR permeability imaging is done particularly in antiangiogenesis protocols with 3D axial T1 dynamic contrast enhanced sequences which with kinetic modeling yield permeability (Kps) and CBV measurements. A modified Tofts model is used (2-compartment, bi-directional flux) to estimate both fractional blood volume (fBV) and microvascular permeability (Kps). DCE permeability MRI metrics also include the volume transfer constant between plasma and extravascular extracellular space (Ktrans),

fractional blood-plasma volume (Vp), and the volume of the extravascular extracellular space per unit volume tissue (Ve).

F. Positron Emission Tomography (PET)

PET imaging is used for evaluation of drug distribution and metabolism, to assess metabolic activity in brain tumors, to assess tumor progression, radiation necrosis and treatment-associated changes in tumor metabolism.

Standard PET procedures are available for those sites having PET capabilities. As a high degree of anatomic localization is required, the PET images are co-registered with MRI data on a workstation used for registration and analysis (Hermes Medical Solutions, Stockholm, Sweden) and converted to Interfile 3.3 image format (See Form 4). Specific PET information is recorded by the site at submission of the PET study (See Form 14 PET support form).

G. PBTC Imaging Protocol Tables

Tables 7 and 8 below outline each PBTC study protocol and the neuroimaging studies that must be completed for that protocol. Study patients are scheduled for their procedure by the site P.I. and the requisition clearly marked to indicate that this is a PBTC study patient along with the PBTC Study Protocol Number in which the patient is enrolled. It should be noted that if more than one neuroimaging study is required and all sequences cannot be completed due to unforeseen circumstances, the priority of MR measurements are as follows: 1) standard MR sequences 2) MR diffusion, 3) MR perfusion, 4) and MR spectroscopy.

Table 7: PBTC Protocols [001 – 009]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-001	A Pilot Study of Systemic and Intrathecal Chemotherapy followed by Conformal Radiation for Infants with Embryonal Intracranial Central Nervous System Tumors	None	Study completed	No correlative objective. Estimate PFS, pattern of failure. Central review of MRI scan at end of study
PBTC-002	A Phase I Study of SU5416 in Pediatric Patients With Recurrent or Progressive Poor Prognosis Brain Tumors	Stratum 1: Patients not on enzyme-inducing anticonvulsant drugs Stratum 2: Patients receiving enzyme-inducing anticonvulsant drugs	Study completed	To identify the signal characteristics and biologic correlates of tumors after SU5416 treatment.
PBTC-003	A Phase I Trial of Escalating Oral Doses of SCH 66336 in Pediatric Patients with Refractory or Recurrent Brain Tumors	None	Study completed	No correlative objective. MRI for response only. No central review.
PBTC-004	A Phase I Study of Intrathecal Spartaject™-Busulfan in Children with Neoplastic Meningitis	None	Study completed	No correlative objective. MRI for response only with central review
PBTC-005	A Phase I Trial of Temozolomide and O^6-Benzylguanine in Pediatric Patients with Recurrent Brain Tumors	Stratum 1: patients previously not treated with RT or only focal RT Stratum 2: patients with prior craniospinal irradiation or myeloblative therapy.	Study completed	No correlative objective. MRI for response only with central review
PBTC-006	A Phase I/II Trial of STI571 in Children with Newly Diagnosed Poor Prognosis Brainstem Gliomas and Recurrent Intracranial Malignant Gliomas	Stratum 1: newly diagnosed localized brainstem tumors Stratum 2A: recurrent intracranial malignant gliomas - not using EIACD Stratum 2B: recurrent intracranial malignant gliomas - using EIACD	Study completed	To develop exploratory data concerning surrogate endpoints of therapeutic activity, using physiological neuroimaging studies and correlative biological studies
PBTC-007	A Phase I/II Trial of ZD1839 (Iressa™) and Radiation in Pediatric Patients Newly Diagnosed with Brain Stem Tumors or Incompletely Resected Supratentorial Malignant Gliomas with Phase II Limited to Brain Stem Tumors	Stratum 1: Newly diagnosed intrinsic brain stem glioma or incompletely resected supratentorial malignant gliomas not receiving enzyme-inducing anti-convulsant drugs Stratum 2: Incompletely resected supratentorial malignant gliomas receiving enzyme-inducing anti-convulsant drugs	Study completed	To compare hemodynamic MR parameters to metabolic FDG-PET scanning and correlate both with clinical response or progression in this population
PBTC-009	A Phase I Trial of GLIADEL® and O^6-Benzylguanine in Pediatric Patients with Recurrent Malignant Gliomas	None	Study completed	MRI / MRS / MR perfusion & diffusion for assessment of response and toxicity

*If neutropenia is the dose limiting toxicity, additional patients will be accrued allowing the use of G-CSF to establish whether higher doses of temozolomide can be administered with this form of hematological support (Stratum 1b &/or 2b)

Table 7: PBTC Protocols [010 – 016]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-010	A Phase II Study of Oxaliplatin in Children with Medulloblastoma, Supratentorial Primitive Neuroectodermal Tumors and Atypical Teratoid Rhabdoid Tumors after Failure of Initial Therapy	Stratum IA: medulloblastoma patients with measurable disease Stratum IB: medulloblastoma patients with only positive CSF cytology or with linear leptomeningeal disease; Stratum II: will include patients with supratentorial primitive neuroectodermal tumor (S-PNET) including pineoblastomas, and ependymoblastomas; Stratum III: patients with atypical teratoid rhabdoid tumors (ATRT).	Study completed	No correlative objective. MRI for response only with central review.
PBTC-011	A Phase I/II Trial of Intracerebral IL13-PE38QQR Infusions in Pediatric Patients with Recurrent Malignant Glioma	No strata in Phase I	Study completed	No correlative objective. MRI for response only with central review.
PBTC-012	A Phase I Study of Cilengitide (EMD 121974) in Children with Refractory Brain Tumors	No strata	Study completed	MRI, MRS, MR perfusion, PET for tumor blood flow, metabolic activity and volume.
PBTC-013	A Phase I/II Study of a Recombinant Chimeric Protein Composed of Transforming Growth Factor (TGF)-□ and a Mutated Pseudomonas Exotoxin Termed PE38 (TP-38) in Pediatric Patients with Recurrent or Progressive Supratentorial High Grade Gliomas	No strata	Study completed	No correlative objective. MRI for response only with central review.
PBTC-014	A Phase I/II Trial of R115777 and Radiation in Pediatric Patients Newly Diagnosed Non-disseminated Intrinsic Diffuse Brainstem Gliomas	No strata	Study completed	To characterize radiographic changes using MRI, MRS, perfusion and diffusion imaging and PET scans.
PBTC-015	A Phase II Trial of 06-Benzylguanine and Temozolomide in Pediatric Patients with Recurrent or Progressive High-Grad Gliomas and Recurrent or Progressive Brainstem Tumors	Stratification Patients will be stratified according to tumor type: Stratum A Recurrent or progressive high grade gliomas Stratum B Recurrent or progressive brain stem tumors	Study completed	To evaluate changes in MR spectroscopic patterns, MR diffusion and MR perfusion in children with refractory or recurrent high-grade gliomas or brainstem gliomas who are treated with the combination of O6-BG and TMZ.
PBTC-016	A Phase I, Molecular Biology and Phase II Study of Lapatinib (GW572016) in Pediatric Patients with Recurrent or Refractory Medulloblastoma, Malignant Glioma or Ependymoma	Phase I: Stratum 1: those who are not receiving steroids; Stratum 2: those who are receiving steroids;	Study completed	To characterize radiographic changes using MRI, MRS, perfusion and diffusion imaging and PET scans.

Table 7: PBTC Protocols [017 – 021]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-017	A Phase I Study of CLORETAZINE™ (VNP40101M) in Children with Recurrent, Progressive or Refractory Primary Brain Tumors	Stratum 1: no prior XRT or focal XRT only and/or < 2 prior myelosupressive chemotherapy regimens; Stratum 2: prior craniospinal XRT, high-dose chemotherapy, and/or > 2 prior myelosupressive chemotherapy regimens	Study completed	No correlative component. Central review for response based on the first MRI scan obtained after 2 courses of chemotherapy.
PBTC-018	A Phase I Trial of CC-5013 in Pediatric Patients with Recurrent or Refractory Primary CNS Tumors	No strata	Study completed	1. To evaluate changes in circulating endothelial cells, circulating endothelial cell precursors, and angiogenic modulators and correlate these changes with changes in MR perfusion and clinical outcome. 2. To evaluate changes in MR spectroscopy, MR perfusion and diffusion during treatment.
PBTC-019	A Phase I Pharmacokinetic Optimal Dosing Study of Intrathecal Topotecan for Children with Neoplastic Meningitis	No strata	Study completed	MRI central review for treatment effects and response at study completion.
PBTC-020	A Phase I Clinical Trial of AZD2171 in Children with Recurrent or Progressive Central Nervous System (CNS) Tumors	Stratum 1: Those who are not receiving enzyme inducing anticonvulsant drugs (EIACD) Stratum 2: Stratum 1: Those who are receiving enzyme inducing anticonvulsant drugs (EIACD)	Study completed	1. To explore correlations in changes in CECs, CEPs and angiogenic modulators with changes in MR perfusion. 2. To obtain preliminary evidence of biologic activity of AZD2171 by evaluating alterations in tissue perfusion, tumor blood flow and metabolic activity using MR perfusion and diffusion imaging, MRS as well as PET analysis and correlating these findings with changes in tumor size by standard MRI. 3. To continue the PBTC investigation of imaging assessments of antiangiogenesis effects by combining data from this trial with other PBTC trials of similar agents.
PBTC-021	A Phase I Trial of Capecitabine Rapidly Disintegrating Tablets and Concomitant Radiation Therapy in Children with Newly Diagnosed Brainstem Gliomas and High Grade Gliomas	No strata	Study completed	To characterize radiographic changes in non-disseminated, newly diagnosed intrinsic brainstem gliomas and high-grade gliomas treated with radiation and capecitabine using MRI, MRS, perfusion and diffusion imaging and PET scans

Table 7: PBTC Protocols [022 – 025]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-022	Phase II study of Bevacizumab plus Irinotecan (Camptosar™) in Children with Recurrent, Progressive, or Refractory Malignant Gliomas, Diffuse/Intrinsic Brain Stem Gliomas, Medulloblastomas, Ependymomas and Low Grade Gliomas	Stratum A: Recurrent, progressive or refractory high-grade gliomas Stratum B: Recurrent, progressive or refractory Intrinsic brain stem tumors Stratum C: Recurrent or progressive Medulloblastomas Stratum D: Recurrent or progressive Ependymomas Stratum E: Recurrent low grade gliomas	Study completed	1. To document changes in MR perfusion and diffusion scans obtained within 24-48 hours following the 2nd dose of Bevacizumab as compared to baseline and correlate with response. 2. To correlate functional changes in tumor with responses to treatment with Bevacizumab + irinotecan using MR perfusion/diffusion imaging, and Fluoro-deoxyglucose (FDG) positron emission tomography (PET). 3. To estimate vascular endothelial growth factor receptor-2 (VEGF-R2) expression in peripheral blood mononuclear cells (PBMC) prior to treatment and its down-regulation following two doses of single-agent Bevacizumab and correlate this finding with permeability changes in the tumor on MR perfusion imaging obtained 24-48 hours following the 2nd dose Bevacizumab
PBTC-023	Phase I and Pharmacokinetic Study of Enzastaurin (LY317615) in Children and Adolescents with Refractory Primary CNS Tumors	No strata	Study completed	To explore changes in correlative magnetic resonance imaging in children receiving enzastaurin. Specifically to evaluate changes in MR perfusion and diffusion scans obtained within 15 ± 2 days after initiation of enzastaurin therapy as compared to baseline and to correlate these changes with clinical outcome, as applicable. 1. Results of imaging studies will be combined across similar PBTC protocols to increase the power for detecting correlations among scans and with outcome.
PBTC-024	A Phase I Study of MK-0752 in Pediatric Patients with Recurrent or Refractory CNS Malignancies	No strata	Study completed	To explore changes in correlative magnetic resonance imaging in children receiving MK-0752. Volumetric MR imaging findings may be combined across similar PBTC protocols to increase the power for detecting correlations among scans and associations with outcome.
PBTC-025	A Phase I Pharmacokinetic and Safety Study in Children with Recurrent or Refractory Medulloblastoma to Identify a Pharmacokinetic Based Dose for GDC-0449	No strata	Study completed	Central review of MR knee, standard MR brain and spine.

Table 7: PBTC Protocols [025B – 033]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-025B	A Phase I Pharmacokinetic and Safety Study in Children with Recurrent or Refractory Medulloblastoma to Identify a Pharmacokinetic Based Dose for GDC-0449	No strata	Open to accrual	Central review of neuro-imaging studies by neuro-radiologists will be conducted to confirm response only in patients reported by the treating site to have experienced an objective response. MRI of the Brain and spine with and without contrast (brain) and post contrast (spine) will be performed.
PBTC-026	A Feasibility Study of SAHA combined with Isotretinoin and Chemotherapy in Infants with Embryonal Tumors of the Central Nervous System	No strata	Open to accrual	To estimate the preliminary response rate of this approach in patients with measurable residual disease (primary site and/or metastatic sites. Central review of standard MR brain and spine.
PBTC-027	A Phase I Study of ABT-888, an Oral Inhibitor of Poly(ADP-ribose) Polymerase and Temozolomide in Children with Recurrent/Refractory CNS Tumors	No strata	Study completed	No correlative objective. MR for response only.
PBTC-029	Phase I and Pharmacokinetic Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	No strata	Open to accrual	Central review of MR imaging studies. To assess diffusion imaging contributions to tumor behavior (type, grade) and response to therapy.
PBTC-029B	A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	Stratum 1: Patients with non NF-1 associated progressive, recurrent or refractory pilocytic astrocytoma with pre-trial tumor material available and with a BRAF aberration excluding patients with optic pathway glioma. Stratum 2: Patients with non NF-1 associated progressive, recurrent or refractory pilocytic astrocytoma with pre-trial tumor material available and without BRAF aberration excluding patients with optic pathway glioma. Stratum 3: Patients with NF-1 associated progressive, recurrent or refractory low grade glioma (WHO I or II), with or without tissue Stratum 4: Patients with non-NF1 associated progressive, recurrent or refractory optic pathway glioma (OPG) with or without tissue available for BRAF evaluation. Stratum 5: Patients with non NF-1 associated progressive, recurrent or refractory low grade glioma (other than pilocytic astrocytoma or optic pathway glioma) with a BRAF aberration.	Open	To describe MRI characteristics of the tumors before and after treatment to determine if there is an early diffusion indicator of response.

		Stratum 6: Patients with non NF-1 associated progressive, recurrent or refractory low grade glioma (other than OPG) with tissue available for BRAFanalysis who cannot be classified into Stratum 1, 2 or 5 due to inadegquate tissue quality		
PBTC-029C - Retreatment	A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	No strata	Open	To describe MRI characteristics of the tumors before and after treatment to determine if there is an early diffusion indicator of response.
PBTC-030	A Phase II Trial of Capecitabine Rapidly Disintegrating Tablets and Concomitant Radiation Therapy in Children with Newly Diagnosed Brainstem Gliomas	No strata	Study completed	To describe and explore changes in diffusion tensor imaging variables in brainstem gliomas in response to therapy and prior to progression.
PBTC-031	Phase I and Pharmacokinetic Trial of PTC299 in Pediatric Patients with Refractory or Recurrent CNS Tumors	No strata	Study completed	To obtain preliminary evidence of biologic activity of PTC299 by using MR diffusion to assess tumor cellularity.
PBTC-032	A Phase II Clinical Trial Evaluating the Efficacy and Safety of GDC-0449 in Children with Recurrent or Refractory Medulloblastoma	Strata A: Patients without evidence of activation of Hedgehog signaling pathway Strata B: Patients with evidence of activation of Hedgehog signaling pathway	Study completed	MR of the knee: To assess for side effects of this drug on growth cartilage MR of brain/spine: Central review of MR scans of brain and spine will be performed to confirm sustained responses and other clinical events as may be needed.
PBTC-033	A Phase I/II Study of ABT-888, an Oral Poly (ADP-ribose) Polymerase Inhibitor, and Concurrent Radiation Therapy, Followed by ABT-888 and Temozolomide, in Children with Newly Diagnosed Diffuse Pontine Gliomas (DIPG)	No strata	Open	To explore the quantitative MR measures of relative cerebral blood volume (rCBV), vascular permeability (Ktrans, vp, and ve values), and apparent diffusion coefficient (ADC) within the first six months of initiating protocol treatment to correlate with disease outcome and determine whether such metrics differentiate patients with pseudoprogression from those with true early progressive disease.

Table 7: PBTC Protocols [036-045]

Protocol	Title	Strata	Status	Neuroimaging Objective/Test
PBTC-036	A Molecular Biology and Phase II Study of Imetelstat (GRN163L) in Children with Recurrent High-Grade Glioma, Ependymoma, Medulloblastoma/Primitive Neuroectodermal Tumor and Diffuse Intrinsic Pontine Glioma	No strata	Study completed	To assess changes in tumor size, enhancement, and diffusion characteristics.
PBTC-037	A phase I study of intratumoral/peritumoral herpes simplex virus-1 mutant HSV1716 in patients with refractory or recurrent high grade gliomas (HGG)	No strata	Open	1. To evaluate changes in tumor enhancement, quantitative MR measures of tumor 1.1.4perfusion (relative cerebral blood volume (rCBV), ktrans, Vp and Ve values and apparent diffusion coefficient (ADC) in response to HSV1716 injection 2. To evaluate changes in FDG-PET uptake in response to HSV1716 injection. 3. To evaluate changes in tumor choline values using MR spectroscopy in response to HSV1716 injection and further delineate from progressive disease versus pseudo-progression post therapy.
PBTC-039	A Phase II study of Peginterferon alfa-2b (PEGIntron) for pediatric patients with unresectable or recurrent craniopharyngioma	Stratum 1: Patients with progressive unresectable or recurrent craniopharyngiomas treated with surgery alone who have not received radiation therapy. Patients with unresectable craniopharyngiomas (i.e., residual measurable disease following surgical resection) will be enrolled at the time of progression Stratum 2: Patients with progressive or recurrent craniopharyngiomas following radiation therapy.	Open	To compare the protocol specific disease assessment criteria to MacDonald criteria during the first year of treatment in stratum I and at the time of objective response and progressive disease in both strata.
PBTC-041	A Phase I Trial of p28 (NSC745104), a Non-HDM2 mediated peptide inhibitor of p53 ubiquitination in pediatric patients with recurrent or progressive CNS tumors	No strata	Study completed	No correlative objective. MR for response only.
PBTC-042	PBTC-042 Phase I study of CDK 4-6 inhibitor PD-0332991 in children with recurrent, progressive or refractory central nervous system tumors	Stratum A: DIPGs Stratum B: non-brainstem HGGs	Open	No correlative objective MR for response only

PBTC-043	A Phase I Trial of Pomalidomide for children with recurrent, progressive or refractory CNS tumors	Stratum 1: Patients on or off steroids Stratum 2: Patients on steroid, <12 Years Old Stratum 3: Patients off steroid, <12 Years Old Stratum 4: Patients on steroid, >=12 Years Old Stratum 5: Patients off steroid, >=12 Years Old	Open	No correlative response MR for response only
PBTC-045	A Safety and Preliminary Efficacy trial of MK-3475 (pembrolizumab; anti-PD-1) in Children with recurrent, progressive or refractory high-grade gliomas (HGG) and DIPGs.	Stratum A: patients with progressive, recurrent or refractory DIPGs Stratum B: patients with progressive, recurrent or refractory non-brainstem HGGs.	Open	1. To examine the ability of quantitative MR spectroscopy and diffusion/weighted imaging/ADC mapping to provide early assessment of tumor behavior and specifically distinguish pseudoprogression from true progression 2. To explore the use of serial MR permeability (DCE) and MR perfusion (DSC) to determine if elevated rCBV and ktrans can distinguish pseudoprogression from true progression in tumors treated on this protocol
PBTC-047	A Phase I Trial of Panobinostat in Children with Diffuse Intrinsic Pontine Glioma	No Strata	Open	No correlative response. MR for response only Will analyze diffusion and standard MR sequences

Table 8: PBTC Protocols [001 – 013]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectro-scopy	Cister-nogram	MR Spine	Bone Scan	PET	CT
PBTC-001	A Pilot Study of Systemic and Intrathecal Chemotherapy followed by Conformal Radiation for infants with Embryonal Intracranial Central Nervous System Tumors	+				+	+	+		
PBTC-002	A Phase I Study of SU5416 in Pediatric Patients With Recurrent or Progressive Poor Prognosis Brain Tumors	+	+	+	+				+	
PBTC-003	A Phase I Trial of Escalating Oral Doses of SCH 66336 in Pediatric Patients with Refractory or Recurrent Brain Tumors	+					+			
PBTC-004	A Phase I Study of Intrathecal SpartajectTM-Busulfan in Children with Neoplastic Meningitis	+					+			
PBTC-005	A Phase I Trial of Temozolomide and O^6-Benzylguanine in Pediatric Patients with Recurrent Brain Tumors	+					+			
PBTC-006	A Phase I/II Trial of STI571 in Children with Newly Diagnosed Poor Prognosis Brainstem Gliomas and Recurrent Intracranial Malignant Gliomas	+	+	+	+		+		+	
PBTC-007	A Phase I/II Trial of ZD1839 (Iressa™) and Radiation in Pediatric Patients Newly Diagnosed with Brain Stem Tumors or Incompletely Resected Supratentorial Malignant Gliomas with Phase II limited to Brain Stem Tumors	+	+	+					+	
PBTC-009	A Phase I Trial of GLIADEL® and O^6-Benzylguanine in Pediatric Patients with Recurrent Malignant Gliomas	+	+	+	+					
PBTC-010	A Phase II Study of Oxaliplatin in Children with Recurrent or Refractory Medulloblastoma, Supratentorial Primitive Neuroectodermal Tumors and Atypical Teratoid Rhabdoid Tumors	+					+			
PBTC-011	A Phase I/II Trial of Intracerebral IL13-PE38QQR Infusions in Pediatric Patients with Recurrent Malignant Glioma	+								+
PBTC-012	A Phase I Study of Cilengitide (EMD 121974) in Children with Refractory Brain Tumors	+		+	+		+		+	
PBTC-013	A Phase I/II Study of a Recombinant Chimeric Protein Composed of Transforming Growth Factor (TGF)-a and a Mutated Form of the Pseudomonas Exotoxin Termed PE38 (TP-38) in Pediatric Patients with Recurrent or Progressive Supratentorial High Grade Gliomas	+								+

Table 8: PBTC Protocols [014-022]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectroscopy	Cister-nogram	MR Spine	Bone Scan	PET	CT
PBTC-014	A Phase I/II Trial of R115777 and Radiation in Pediatric Patients Newly Diagnosed Non-disseminated Intrinsic Diffuse Brainstem Gliomas	+	+	+			+		+	
PBTC-015	A Phase II Trial of 06-Benzylguanine and Temozolomide in Pediatric Patients with Recurrent or Progressive High-Grad Gliomas and Recurrent / Progressive Brainstem Tumors	+		+	+				+	
PBTC-016	A Phase I, Molecular Biology and Phase II Study of Lapatinib (GW572016) in Pediatric Patients with Recurrent or Refractory Medulloblastoma, Malignant Glioma or Ependymoma	+	+	+			+		+	
PBTC-017	A Phase I Study of CLORETAZINE™ (VNP40101M) in Children with Recurrent, Progressive or Refractory Primary Brain Tumors	+					+			
PBTC-018	A Phase I Trial of CC-5013 in Pediatric Patients with Recurrent or Refractory Primary CNS Tumors	+	+	+			+		+	
PBTC-019	A Phase I Pharmacokinetic Optimal Dosing Study of Intrathecal Topotecan for Children with Neoplastic Meningitis	+					+			
PBTC-020	A Phase 1 Clinical Trial of AZD2171 in children with Recurrent or Progressive Central Nervous System (CNS) Tumors	+	+	**T1 permeability followed by T2***			+		+	
PBTC-021	A Phase I Trial of Capecitabine Rapidly Disintegrating Tablets and Concomitant Radiation Therapy in Children with Newly Diagnosed Brainstem Gliomas and High Grade Gliomas	+	+	+			+		+	
PBTC-022	Phase II study of Bevacizumab plus Irinotecan (Camptosar™) in Children with Recurrent, Progressive, or Refractory Malignant Gliomas, Diffuse/Intrinsic Brain Stem Gliomas, Medulloblastomas, Ependymomas and Low Grade Gliomas	+	+	**T1 permeability followed by T2***			+		+	

Table 8: PBTC Protocols [023-032]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectroscopy	Cister-nogram	MR Spine	Bone Scan	PET	CT
PBTC-023	A Phase I and Pharmacokinetic Study of Enzastaurin (LY317615) in Children and Adolescents with Refractory Primary CNS Tumors	+	+	**T1 permeability followed by T2***			+			
PBTC-024	A Phase I Study of MK-0752 in Pediatric Patients with Recurrent or Refractory CNS Malignancies	+					+			
PBTC-025	A Phase I Pharmacokinetic and Safety Study in Children with Recurrent or Refractory Medulloblastoma to Identify a Pharmacokinetic Based Dose for GDC-0449 **	+					+			
PBTC-025B	A Phase I Pharmacokinetic and Safety Study in Children with Recurrent or Refractory Medulloblastoma to Identify a Pharmacokinetic Based Dose for GDC-0449	+					+			
PBTC-026	A Feasibility Study of SAHA combined with Isotretinoin and Chemotherapy in Infants with Embryonal Tumors of the Central Nervous System	+					+			
PBTC-027	A Phase I Study of ABT-888, an Oral Inhibitor of Poly(ADP-ribose) Polymerase and Temozolomide in Children with Recurrent/Refractory CNS Tumors	+					+			
PBTC-029	A Phase I and Pharmacokinetic Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	+	+				+			
PBTC-029B	A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	+	+				+			
PBTC-029C - Retreatment	A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma	+	+				+			
PBTC-030	A Phase II Trial of Capecitabine Rapidly Disintegrating Tablets and Concomitant Radiation Therapy in Children with Newly Diagnosed Brainstem Gliomas *	+	+							
PBTC-031	A Phase I and Pharmacokinetic Trial of PTC299 in Pediatric Patients with Refractory or Recurrent CNS Tumors	+	+				+			
PBTC-032	A Phase II Clinical Trial Evaluating the Efficacy and Safety of GDC-0449 in Children with Recurrent or Refractory Medulloblastoma	+					+			

Table 8: PBTC Protocols [033-045]

Protocol	Trial	MR Brain	MR Diffusion	MR Perfusion	MR Spectroscopy	Cister-nogram	MR Spine	Bone Scan	PET	CT
PBTC-033	A Phase I/II Study of ABT-888, an Oral Poly (ADP-ribose) Polymerase Inhibitor, and Concurrent Radiation Therapy, Followed by ABT-888 and Temozolomide, in Children with Newly Diagnosed Diffuse Pontine Gliomas (DIPG)	+	+	**T1 permeability followed by T2***			+			
PBTC-036	A Molecular Biology and Phase II Study of Imetelstat (GRN163L) in Children with Recurrent High-Grade Glioma, Ependymoma, Medulloblastoma/Primitive Neuroectodermal Tumor and Diffuse Intrinsic Pontine Glioma	+	+				+			
PBTC-037	A phase I study of intratumoral/peritumoral herpes simplex virus-1 mutant HSV1716 in patients with refractory or recurrent high grade gliomas (HGG)	+	+	+	+				+	
PBTC-039	A Phase II study of Peginterferon alfa-2b (PEGIntron) for pediatric patients with unresectable or recurrent craniopharyngioma	+								
PBTC-041	A Phase I Trial of p28 (NSC745104), a Non-HDM2 mediated peptide inhibitor of p53 ubiquitination in pediatric patients with recurrent or progressive CNS tumors	+	+				+			
PBTC-042	Phase I study of CDK 4-6 inhibitor PD-0332991 in children with recurrent, progressive or refractory central nervous system tumors.	+					+			
PBTC-043	A Phase I Trial of Pomalidomide for children with recurrent, progressive or refractory CNS tumors	+	+				+			
PBTC-045	A Safety and Preliminary Efficacy trial of MK-3475 (pembrolizumab; anti-PD-1) in Children with recurrent, progressive or refractory high-grade gliomas (HGG) and DIPGs	+	+	+	+		+			
PBTC-045	Phase 1 Trial of Panobinostat in Children with Diffuse Intrinsic Pontine Glioma	+	+							

* DTI
** MR of knee required

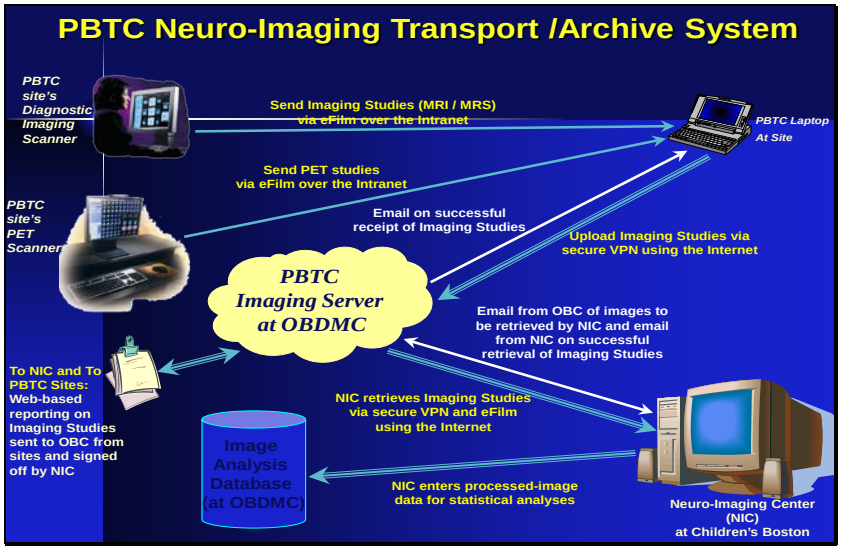
Section IV
PBTC NIC Manual of Operations Procedures for Transfer of Imaging Studies

IV. Procedures for Transfer of Imaging Studies

A. MR and PET Image Transfer

The PBTC neuroimaging studies are sent across a secure tunnel from the participating sites to the OBDMC at St. Jude's Hospital and then to the Neuroimaging Center at Boston Children's Hospital. Software in the Operations Office is used to replace the patient identifiers with PBTC codes. It is important that the patient identifiers are stripped and replaced with PBTC codes at the central Operations office, as it not only maintains patient confidentiality before the studies are sent to the Neuroimaging Center of the PBTC; it also provides us with the accountability to match correct patient data with the imaging studies. Throughout the transmission process from the PBTC sites to the Operations Office of PBTC and then onwards to the Neuroimaging Center of PBTC, the OBDMC is employing a Virtual Private Network (VPN) solution. The data are highly encrypted and encapsulated in this secure tunnel. This VPN solution has been used to transmit the PBTC database that has all patient information from the PBTC sites to the Operations Office. The OBDMC staff is fully aware of the HIPAA regulations and has made sure that the Operations Office conforms to the HIPAA regulations in their work for the Consortium.

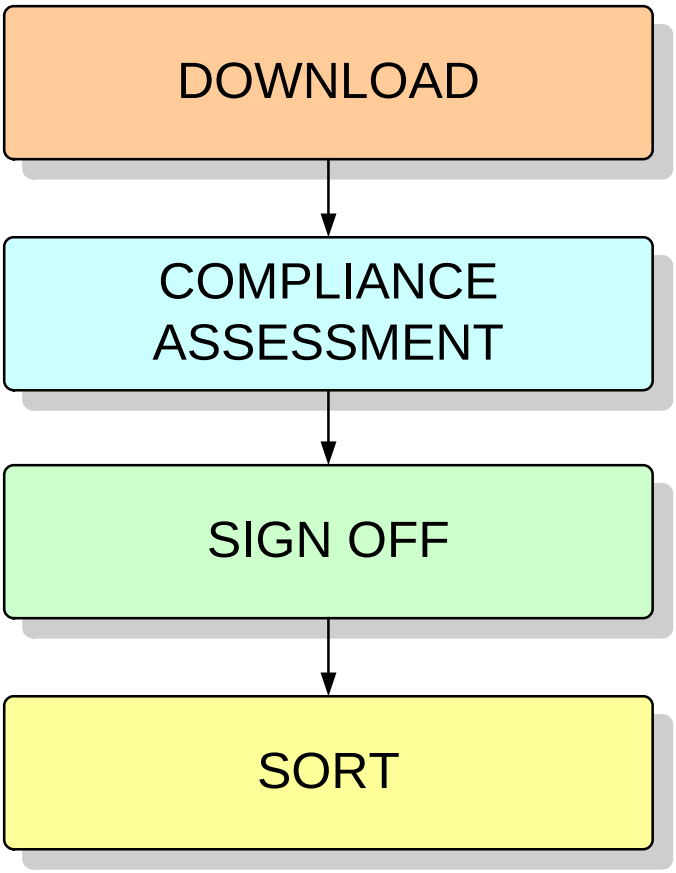
MR and PET studies are downloaded from the OBDMC after email notification to the NIC. This is followed by a compliance assessment, followed by the completion of a web-based form to indicate that download is completed, and a sign-off procedure on each designated series of the exam for presence and analyzability. The studies are sorted into the appropriate protocol folder on the NIC PC workstation and backed up to the PBTC NIC server.



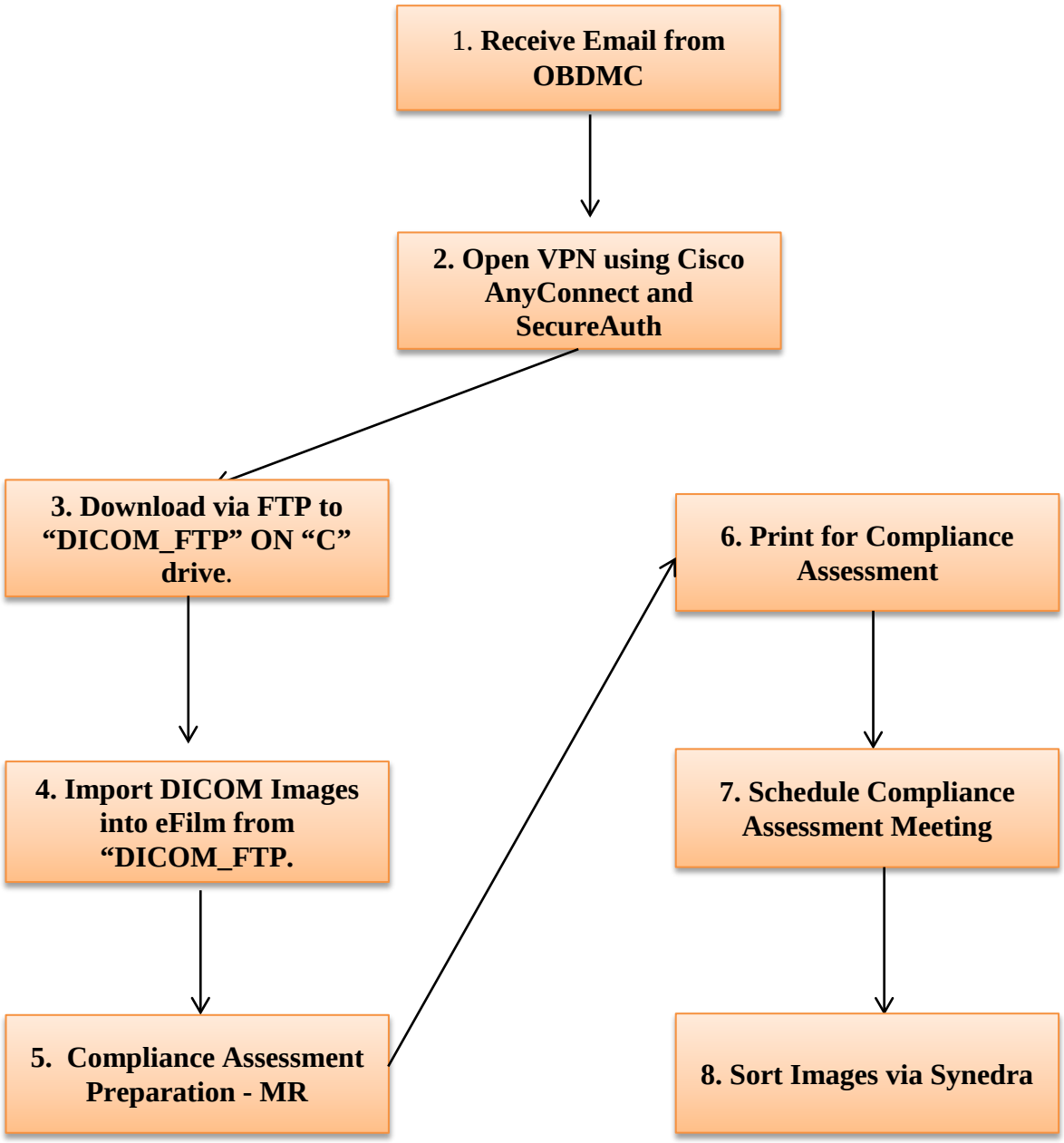
B. PBTC NIC Operations Overview for MR & PET Image Manipulation

The process of downloading, compliance assessment, sign-off and sorting is described as follows in stepwise outline form.

PBTC NIC OPERATIONS OVERVIEW FOR MR AND PET IMAGE MANIPULATION



I. From Download to Sorting



I. - Download

1 - Receive email from the OBDMC

- Email will contain where studies are located on the FTP server
  - Download date specific folder name
  - Special notes and/or circumstances

2 - VPN Client Access

- All download procedures require an active VPN connection between St. Jude's OBDMC and Boston Children's Hospital, NIC.
- Open *Cisco AnyConnect Secure Mobility Client*
  1. Username: [**Insert Here**]
     Password: [**Insert Here**]
  2. Open SecureAuth
     Enter PIN
     Input second password to Cisco
     Accept Banner

3 - Download via FTP

- Open *Filezilla Client*
- Connect to "remote browser"
  1. Remote server IP = **[Insert Here]**
  2. Log-in set to **[Insert Here]**
- The OBDMC will supply the folder name of the download in an email.
- Copy files from OBDMC Server to NIC Workstation folder "DICOM_FTP" [**C:\PBTC_Download\DicomFTP**]

4a - Compliance Assessment Preparation - MR

- Open Excel
- File open; [C:\\PBTC Download-Signoff.xls]
  1. File should open to "download raw MR" tab, if not switch to that tab.
- Open "Internet Explorer."
- Open "PBTC Web Report"
  http://10.38.48.102/PBTC_WebReport/I8M1A3G9E7D1U6K2E9/default.html

- Log-in
    1. OBDMC has provided personal usernames and passwords.
- Mouse-click the “click here” link attributed to “To sign-off downloaded MRI/MRD/MRP/MRS/CT studies on OBDMC server, please click here**.**”
- A new browser window will open.
- Highlight the MR spreadsheet that appears and copy.
    1. Important: Be sure to omit the header rows when copying MR data. Header rows are provided in the Excel file.
- Return to Excel
- Paste MR data onto the “download raw MR” tab.
    1. Be sure that data is pasted in the first free cell of the first column. [A4]
    2. The drop-down menus the data may take a few minutes to appear.
- Once loaded, copy the MR data from “Download Raw MR” tab.
- Paste in the “download format MR” tab.
- Format MR page for printing
    1. “Find all” for “institution.”
    2. Replace all “institution” with “inst.”
    3. Decrease the width of “confirmed by.” [J] to 3.00
    4. Reformat cells under column header name, “scan date.” [C]
        - Data column should be formatted to “dd/mm/yy”
    5. Remove column with header name, “Phase ID.” [E]
    6. Remove column with header name, “Images downloaded & components confirmed during previous upload.” [G]
        7. Remove column with header name, “Components Confirmed during Previous Upload.” [G]
    8. Remove column with header name, “comments.” [I]
    9. Change fill color for all columns with the header name “analyzable” to “light yellow” [J, L, O, R, T, V, X, Z, AC, AE, AG, AI, AK].
    10. Change fill color for columns with the header names of “Diffusion.” “T2* Perf”, “T1 Perm Perf”, “Spec Sing”, “DTI” to “light grey” [S, U, W, and Y respectively].
    11. View “page break preview.”
        - Entire spreadsheet should fit in landscape on legal-sized paper.
        - Be sure page break does not interrupt length or width of data columns or rows.
    12. View “print preview.”
        - Be sure that records do not cut off or interfere with the footer.
    13. “Save as” date of OBDMC email.

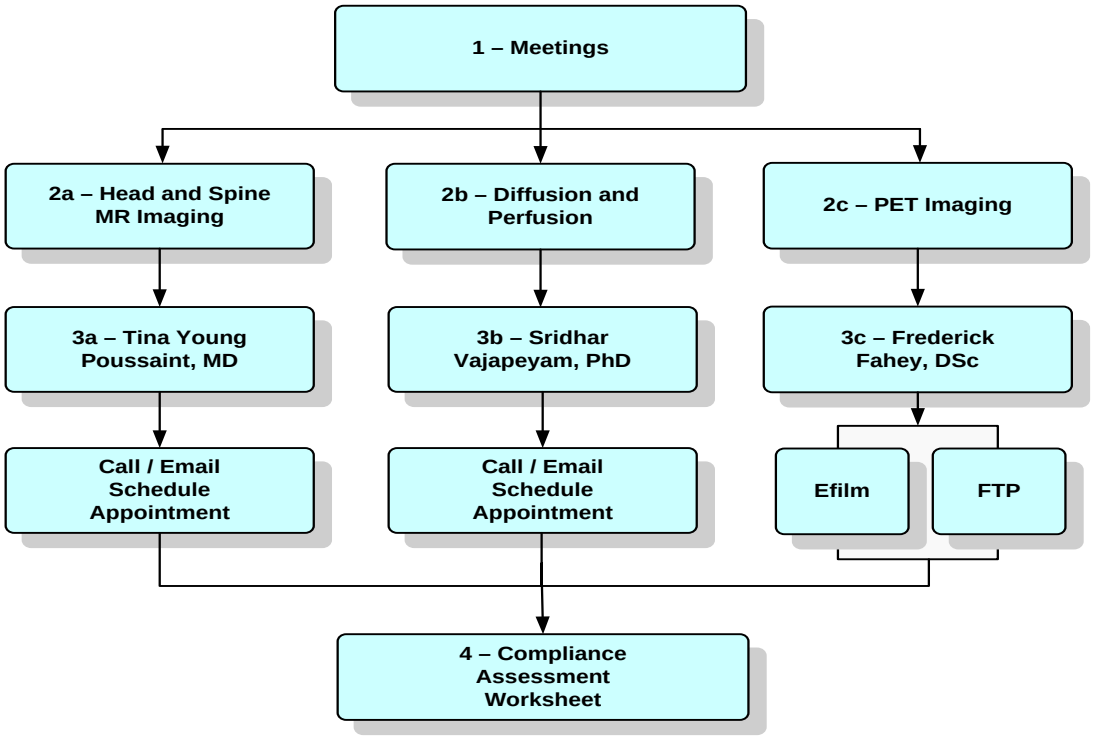
4b - Compliance Assessment Preparation - PET

- Return to *Internet Explorer* and the web report.
- Mouse-click the “click here” link attributed to “To sign-off downloaded PET studies on OBDMC server, please click here.” A new browser tab will open.
- Highlight the entire spreadsheet **including** headers, and copy.
- Return to Excel
- Paste PET Data in the “Download Raw PET” tab.
  1. Be sure that data is pasted in the first free cell of the first column. [A1]
  2. The drop-down menus the data may take a few minutes to appear.
- Once loaded, copy the PET Data from the “Download Raw PET” tab.
- Paste in the “Downloaded Format PET” tab.
- Save

5 – Print

Sign-off worksheets require the use of legal-sized printer paper (11” x 14”) and can easily be printed using network printer “lwc05mfp04.”

II. COMPLIANCE ASSESSMENT



II. - Compliance Assessment

1 - Meetings

- There are three types of scans in each download:
  1. Head and spine MR imaging
  2. Diffusion, Perfusion and Spectroscopic Imaging
  3. PET imaging
- Each type of scan requires the review of a different specialist.
  1. Tina Young Poussaint, MD
     - Call/email and schedule an appointment to meet.
  2. Sridhar Vajapeyam Ph.D.
     - Call/email and schedule an appointment to meet.
  3. Frederick Fahey D.Sc.
     - Copy "Download Format PET" spreadsheet and paste it into an email.
       1) If PET studies were downloaded via eFilm, he will view images via a pre-existing sharing function in eFilm.

2 - The Compliance Assessment Worksheet

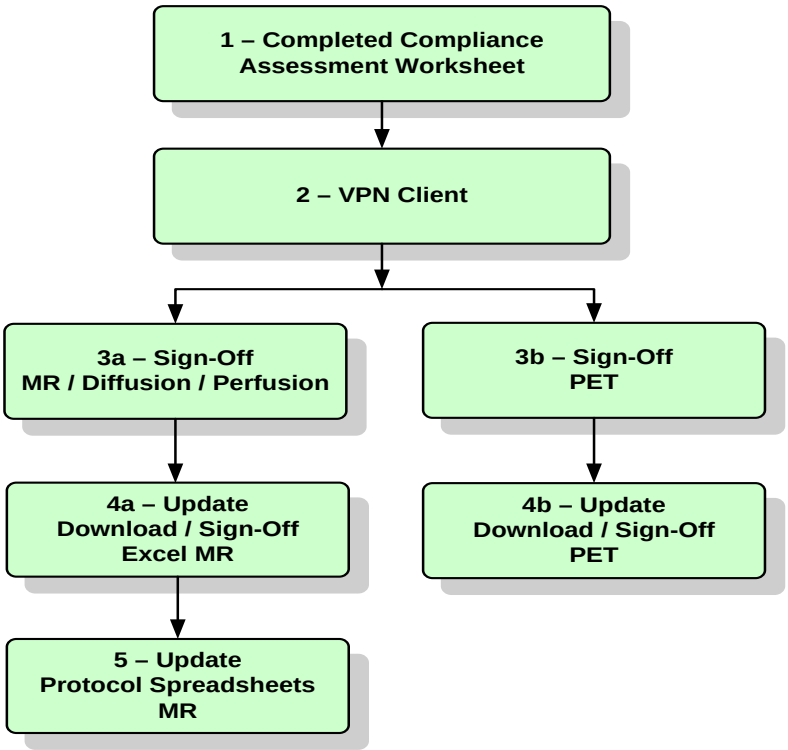
- Filling out the component portion of the sign-off sheet—
  1. Components received by the NIC should match those sent by the institution.
     - If this is the case, check the box.
     - If this is NOT the case, cross out the institution and confirmation. Write in the corrected value.
  2. If all components are present—
     - Write "all" in the column with the header name, "Images downloaded & components confirmed."
     - Write "no" in the column with the header name, "Re-upload needed?"
  3. If not all components are present—
     - Write "some" in the column with the header name, "Images downloaded & components confirmed."
     - The study may need re-uploading, depending on the component missing. Check "Tables 7 and 8: PBTC Protocols", to see which components are mandatory for which protocol.

4. If none of the components are present—
    - Write “none” in the column with the header name, “Images downloaded & components confirmed”.
    - Write “yes” in the column with the header name “Re-upload needed?”

5. If Components are present but not listed, hand-write a comment stating such—
    - Filling out the analyzability portion of the sign-off sheet:
        1) If a component is analyzable, check the box.
        2) If a component is not analyzable, write “no”
    - Scans that are not analyzable do not require re-upload.

- Comments
    1. Comments should be made on the PBTC Assessment Sheet and transcribed during the sign-off process.
    2. Comments should be separated into “OBDMC Comments,” “Site,” and “NIC” comments.
- OBDMC – Notes to command the attention of the OBDMC
- Notes to command the attention of the Sites themselves.
- NIC – Notes for internal use only

III. SIGN-OFF



III. Sign-off

1 - Completed Compliance Assessment Forms

- All three scan types must be reviewed by the appropriate specialist prior to sign-off.
  - MR
  - Diffusion/Perfusion/Spectroscopy
  - PET
- The completed Compliance Assessment Worksheet should make note of the following:
  1. The download received is compliant with the study list provided by the OBDMC.
  2. The studies are compliant with their respective protocols.
  3. Studies that are present are analyzable.
  4. Missing or incomplete studies that require a re-upload request.
  5. Itemized comment list of any incidental cases that may have been downloaded but not tracked by the sites.

2- VPN Client Access

- All download procedures require an active VPN connection between St. Jude's OBDMC and Boston Children's Hospital, NIC.
- Open *Cisco AnyConnect Secure Mobility Client*
  1. Username: [**Insert Here**]
     Password: [**Insert Here**]
  2. Open SecureAuth
     Enter PIN
     Input second password to Cisco
     Accept Banner

3a Sign-off Procedure for MR/Diffusion/Perfusion/Spectroscopy studies

- Open Internet Explorer
- Open favorite site: "PBTC Web Report"
  http://10.38.48.102/PBTC_WebReport/I8M1A3G9E7D1U6K2E9/default.html]
- Log-in
  1. OBDMC has provided personal usernames and passwords.

- Mouse-click the “click here” link attributed to “To sign-off downloaded MRI/MRD/MRP/MRS/CT studies on OBDMC server, please click here**”** on the OBDMC web report.
- A new browser window will open.
- Transcribe the data collected on the Compliance Assessment Worksheet during the Compliance Assessment Meetings into the component portion of the sign-off web report.
- If *all* of the components uploaded by the institution are confirmed with institution's information, please select "yes, all" in the column with the header name, “Images downloaded & components confirmed.”
    1. By selecting “yes, all” you are automatically populating the “yes” to every “component” column offered on the web report.
    2. Be aware that by selecting “yes, all” you are self-populating the “Re-upload needed?” column with a “no” response.
    3. When a “yes, all” selection does <u>not</u> populate the “analyzable” column, it will require manual population.
- If *some* of the components uploaded by the institution are confirmed with institution's information, please select "yes, some" in the column with the header name, “Images downloaded & components confirmed.”
    1. By selecting “yes, some” you need to manually populate each “yes/no” drop-down menu for each component column on the web report.
    2. Be aware that by selecting “yes, some,” the “Re-upload needed?” column will not self-populate and thus, will need to be manually populated.
        - The study may need re-uploading depending on the component and the protocol. Check “Tables 7 and 8: PBTC Protocols” to see which components are mandatory for which protocols.
    3. When a “yes, some” selection does <u>not</u> populate the “analyzable?” column, it will require manual population.
- If *none* of the components uploaded by the institution are confirmed with institution's information, please select "no, none" in the column with the header name, “Images downloaded & components confirmed.”
    1. By selecting “no, none,” you are automatically populating the “no” to every component column offered on the web report.
    2. Be aware that by selecting “no, none,” you are self-populating the column with the header name “Re-upload needed?” with a “yes” response.
    3. A “no, none” selection will self-populate the “analyzable?” columns to “no.”

4. “No, none” selection requires a reason comment for reupload comment.

- If components are present, but not listed by the OBDMC, hand-key an NIC comment in the “comments” column stating such.
- Click the “sign-off neuro-imaging studies downloaded from OBDMC Server” button at the very bottom of the MRI/Diffusion/Perfusion sign-off page.
  1. Blank value will result in an error message.
- A new browser window will open with a summary of the just submitted data.

3b - Update Download/Sign-off Excel for MR/Diffusion/Perfusion/Spectroscopy

- Open Excel
- File open; [C:\PBTC Download-Signoff.xls]
  1. File should open to the “Download Raw MR” tab.
  2. Select “Sign-off MR” tab.
- Return to “Internet Explorer” and the web report submission summary page.
- Highlight the most recent data, omitting the header rows.
- Right mouse-click to copy.
- Return to Excel file [PBTC Download-Signoff.xls]
- Paste the new data into the left uppermost free cell. [A4]
- Save.

4a - Sign-off Procedure for PET Studies

- Open Internet Explorer.
- Open favorite site: “PBTC Web Report.”
- http://10.38.48.102/PBTC_WebReport/I8M1A3G9E7D1U6K2E9/default.html
- Log-in
  1. OBDMC has provided personal usernames and passwords.
- Mouse-click the “click here” link attributed to “To sign-off downloaded PET studies on OBDMC server, please click here.**”**
- If the study was received from the OBDMC by the NIC, select “yes” in the column named “Images downloaded & confirmed.”
  1. Manual population of “Re-upload needed?” & “PET scan analyzable?” required.
- If the study was not received from the OBDMC by the NIC, select “no” in the column named “Images downloaded & confirmed.”

1. Self populates “yes” for “Re-upload needed?” and “no” for “PET scan analyzable?”

- Comments added in designated column as needed.
- Click the “Sign-off Neuro-imaging studies downloaded from OBDMC Server” button at the very bottom of the PET sign-off page.
  1. Blank values will result in an error message.
  2. A new browser window will open with a summary of the just submitted data.

4b - Update Download/Sign-off Excel PET

- Return to Excel.
- File open; [C:PBTC Download-Signoff.xls]
  1. File should open to the “download MR Raw” tab.
  2. Select “Signoff PET” Tab.
- Return to Internet Explorer and the web report submission summary page.
- Highlight the most recent data, including the header rows.
- Right mouse-click to copy.
- Return to Excel file [PBTC Download-Sign-off.xls]
- Paste the new data into the left uppermost free cell. [A1]
- Save.

5 - Update Protocol Spreadsheets - MR

- Open Internet Explorer.
- Open favorite site: “PBTC Web Report.”
  1. [http://10.38.48.102/PBTC_WebReport/I8M1A3G9E7D1U6K2E9/default.html]
- Log in to the *PBTC Web Report.*
  1. OBDMC has provided personal usernames and passwords.
- Locate the “drop-down” menu and “view” button associated with “To view MRI/MRD/MRP/MRS studies sent to OBDMC and downloaded to NIC, in Excel format, select protocol.**”**
  1. Each drop-down menu option will open an Excel file listing of all studies obtained for that protocol by accession number.

- Go to \\rc-fs.tch.harvard.edu\rad-poussaint\Public\R40300\
  2. Username: **[Insert Here]**
     Password: **[Insert Here]**
- Select folder named, “PBTC Protocol Spreadsheets”

- Contained within each protocol-specific folder is a spreadsheet for that protocol:
  [{protocol number}_PBTC-MR-image-Studies-list.xls]
  1. Be aware that some protocols have more than one run, or phases.
  2. An additional phase will be represented by a lower case Roman numeral directly following the {protocol number} in the file name. Ex: 014ii = Protocol 14, Phase 2
  3. A phase breakdown list can be found on the F:\ Drive of the Workstation [\NIC Download Resources\Phase Information]
- Updating the spreadsheets
  1. Compliance Assessment Worksheet
  2. Select the first protocol/accession number listed on the Compliance Assessment Worksheet.
  3. \\rc-fs.tch.harvard.edu\rad-poussaint\Public\R40300\
  4. Open the Excel spreadsheet for that protocol.
  5. Select the dated tab, if the spreadsheet does not automatically open to that tab.
  6. **OBDMC WebReport**
  7. Select that protocol on the drop-down menu of the OBDMC Web Report.
  8. View.
  9. A new browser window will open as well as a "file download – security warning."
  10. Open. This will open the OBDMC version of the spreadsheet in the new browser window.
  11. Using the Compliance Assessment Worksheet as a guide, select the entire row corresponding to the protocol/accession number/date combination for the study in that download.
  12. Copy.

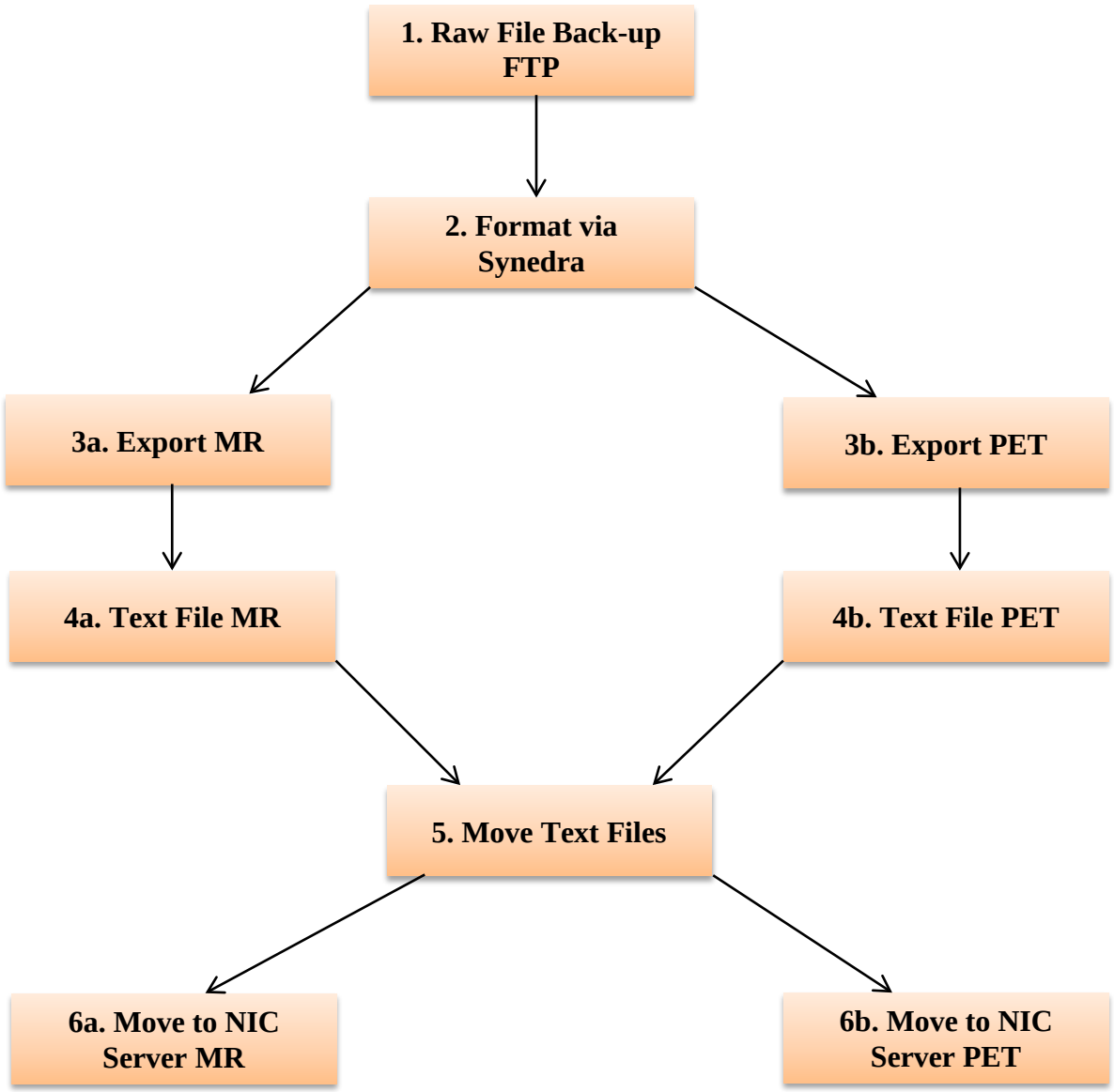
Return to \\rc-fs.tch.harvard.edu\rad-poussaint\Public\R40300\

  13. Return to \\rc-fs.tch.harvard.edu\rad-poussaint\Public\R40300\
  14. Paste the new row in the first open row of the dated tab.
  15. Continue copy/paste until each newly downloaded entry for that protocol is completed.
  16. Rename the worksheet tab on the spreadsheet to reflect the day the update took place.
  17. Continue this process for each protocol, until the entire download has been reflected on the spreadsheets.

- Protocols 020, 022, 023, 030, & 033

1. These protocols, in particular, require two types of perfusion diffusion tensor imaging.(DTI)
   - T2* gradient echo perfusion
   - T1 permeability
   - DTI
2. If it is the case that the values on the sign off page do not reflect the studies received by the NIC for T2* perfusion, T1 permeability or diffusion imaging then short hand notation is used to accurately record the studies received on the Compliance Assessment Worksheet. and this information is then hand keyed into the Protocol Specific spreadsheets.
3. Analyzability data for the perfusion studies will have been recorded on the Compliance Assessment Worksheet.
4. Open Excel [{020/022/023/030/033}_PBTC-MR-image-Studies-list.xls].
5. Select the DTI/Perf tab.
6. Transcribe the analyzability of T2*, T1 permeability, and DTI in their respective hand key (orange) columns.
   - Analyzability is recorded with the following short-hand.
     i. 0 = not present/not analyzable
     ii. 1 = present/not analyzable
     iii. 2 = present/analyzable

IV. SORTING IMAGES



IV. - Sort

1 - Raw File Backup – FTP

- Open the two local browsers:
  1. C:\PBTC_Download\DicomFTP
  2. E:\PBTC Download Backup
     - Create a file with the download date supplied by the OBDMC in the notification email.
- Copy the entire "C:\PBTC_Download\DicomFTP" into "E:\PBTC Download Backup\DoD."
  1. Where DoD = date of download

2 - Format via Synedra

- Files sent from the OBDMC have a numerical dicom file header name. In an effort to avoid confusion during subsequent analysis, the NIC formats each file header name to be alpha-numeric. The NIC uses DICOM Works for this procedure.
- Open *Synedra.*
  1. *Synedra* should be the only application running.
  2. *Synedra* will open to the last directory it had access to. The size of that directory will dictate how long it will take DICOM Works to load. Be patient.

4a - Text File - MR

- Open a *Command Prompt* window.
- The opening directory will be [C:\Documents and Settings\[log in profile name].
- Enter the command [cd ..\..]
  1. Where "cd" = "change directory" and the "..\.." = the number of levels retraced to bring one to the main C:\ directory.
  2. This will bring you to the main C:\ directory.
- Enter the [\PBTC_Download\DicomMrToBeSorted]
- Enter dir > [file name]mr.txt.
  1. The "dir" command creates a text file list of the contents of that directory.

2. The file name should be the “date of the download” [dd-mm-yy].
3. The file name is followed by the file type [MR].
4. The file extension is [.txt].

- Click “enter.”

4b - Text File – PET

- Open a *Command Prompt* window.
- The opening directory will be [C:\Documents and Settings\[log in profile name].
- “Enter” the command [cd ..\..]
  1. Where “cd” = “change directory” and the “..\..” = the number of levels retraced to bring one to the main C:\ directory.
  1. This will bring you to the main C:\ directory.
- Enter the [\PBTC_Download\DicomPetToBeSorted]
- Enter [dir >{file name}pet.txt.
  1. The “dir” command creates a text file list of the contents of that directory.
  2. The file name should be the “date of the download” [dd-mm-yy].
  3. The file name is followed by the file type [PET].
  4. The file extension is [.txt].
- “Enter.”

5 - Move Text Files

- Open a local browser.
  1. NIC Workstation [C:\NIC Download Resources\TxtByDate]
- New folder
- Name folder with date of download.
  1. [dd-mm-yy]
- Open an additional local browser.
  1. Workstation [C:\PBTC_Download\DicomMrToBeSorted].
- Select “DicomMrToBeSorted.”
- Move [filename]mr.txt file to RAD-Poussaint drive.
- Go up one level.
- Select “DicomPetToBeSorted.”
- Move [filename]pet.txt file to NIC Workstation.

6a - Move to the NIC Server – MR

- Open the two local browsers:
  1. Workstation [PBTC_Download\DicomMrToBeSorted]
  2. Server [Poussaint on RC-FS(RC-FS.tch.harvard.edu)]
     - Folders are Protocol Specific
- Move files from the workstation into respective protocol specific folder on the server.
- Repeat until all files in workstation have been moved to the server.

6b - Move to the NIC Server – PET

- Open the two remote browsers:
  1. Workstation [PBTC_Download\DicomPetToBeSorted]
  2. Server [Poussaint on RC-FS(RC-FS.tch.harvard.edu)]]
     - Folders are protocol-specific
- Move files from the workstation into respective protocol specific folder on the server.
- Repeat until all files in workstation have been moved to the server.

MRS Raw Data Transfer

Contact Person: Sridhar Vajapeyam, PhD 617-355-7870;
Email: sridhar.vajapeyam@childrens.harvard.edu
Please note all sites should do a screen save of the MRS spectrum with the ratios displayed on the image.

1.) GE Scanners

- The spectroscopy raw data files are stored in the directory /usr/g/mrraw.
- Open a C shell and go to the directory /usr/g/mrraw by typing the command "cd /usr/g/mrraw."
- List the files in the directory by typing "ls –l."
- You will see several files with names like Pxxxxx.7.
- You will also see the date and time the files were created.
- Pick the right files based on the date and time the MRS study was conducted and copy them to a separate directory and then transfer them to OBDMC of the PBTC.

2.) Siemens Scanners

- The Syngo Database will list the spectroscopy raw data files associated with a study.
- Export these files to a new folder and then transfer them to OBDMC of the PBTC.
- Since Sonata System has no means of writing any data other than patient data (in DICOM format) into a CD ROM, you would have to first export the raw data to a temporary directory. You will then ftp this file to a PC or a Unix workstation for further processing. The data is in Siemens 'rdx' format following export.

Exporting data:

a. Drag raw data into the "spectroscopy task card" just as you would when processing spectroscopy data.

b. Click on "options" on the menu bar and then choose "export raw data".

c. You will be asked for a directory and a file name to export the data.

d. Normally you would use the "C:\temp" Directory. Data now is exported.

ftp data:

a. First log into Windows NT system by holding 'CTRL" and "Esc" keys > together. This will allow you to get access to the Microsoft Windows > environment.

b. Click on "start" button on the lower left corner of the screen, click on "advanced user" if you have not logged into the NT systems previously. This will give you a prompt window for your password input. Factory default password is "meduser1" unless it has been previously altered.

c. After you log into the NT systems, hit "CTRL" and "Esc" simultaneously again. Go to "start" then "programs" and the "command prompt." This will open up a DOS window with a prompt "C:\". Change to "temp" directory (or other directory you created when you export your raw data) by typing "cd temp."

d. You can now ftp your data out to other PC or workstations. Do not forget to set to "binary" mode when you ftp or your data will be garbled.

e. Example: "ftp 123.45.678.99" (connect to your ftp server PC or unix system) (enter user name/password) "bin" (change from ASCII mode to binary) "put file name" (upload data) "quit."

3.) Phillips Scanners

- Raw spectroscopy data and the corresponding header information are stored as .SDAT and .SPAR files associated with the patient identifier.
- The localizer image data and header are stored as .REC and .PAR respectively.
- Transfer all these files for each spectroscopy study into a separate folder and then transfer to OBDMC of the PBTC.

Transfer to OBDMC of the PBTC MRS data will require an ftp connection between the site's scanner workstation and the PBTC laptop. Once the files reach the PBTC laptop at the site, then the CRA at the site can ftp it over the secure channel to OBDMC of the PBTC.

Section V
PBTC NIC Manual of Operations Guidelines for Reading and Interpreting Imaging Studies

V. Guidelines for Reading and Interpreting Imaging Studies

The NIC is responsible for image analysis of all PBTC research neuroimaging studies. Each study is reviewed by 1-2 Neuroradiologists from the NIC and the final interpretation of results reached by consensus.

Before image analysis, imaging studies are evaluated for readability and compliance with the protocol and the protocol compliance form is completed by the data volumetric analyst and data analysis engineer in consultation with the neuroradiologist.

The standard FLAIR, T2, and gadolinium sequences are sent to the Vitrea workstation (Vital Images, Plymouth, MN) and volumetric analysis is done. The data volumetric analyst consults with one of two neuroradiologists to determine the tumor site and regions of interest to be measured. Automated segmentation software defines the tumor regions on FLAIR or T2 images and nonenhancing and enhancing tumor regions on gadolinium T1 axial images. The perfusion, diffusion and MRS components of each study are transferred from the PC workstation to a dedicated workstation for image analysis (see data form MR). After reviewing the post-analysis data, the information is backed up on the NIC workstation, research computing server and a dedicated backup server system through CHB Research Computing.

Section VI
PBTC NIC Manual of Operations
Data Management Procedures

VI. Data Management Procedures

Data is collected on hard copy forms by NIC data analysts, NIC nuclear medicine physicist/physician and neuroradiologists at the time of image analysis. The NIC Research Coordinator, Selby Knudsen, ensures that all necessary data are collected in a timely and efficient fashion. The study coordinator reviews all hard copy data forms and completes data entry at the CRC. The data forms are entered directly through the PBTC web-based data management system and managed by the PBTC Operations and Biostatistics Center. All other data such as quality assurance data are entered into an SPSS database at the CRC. For these data, the CRC generates data entry status reports and generates frequency distributions of study variables to provide timely and relevant feedback to the NIC. A password protected study directory is established on the program's server for all database files and analysis files. Datasets are cleaned, verified, archived with documentation and then used to create documented analysis files. Access to programs and datasets is denied by password to non-study staff. All analytic and database files are backed up daily. No patient identifiers are present in the database or on forms. Each study participant has a unique PBTC assigned study numeric study identifier that includes a site, protocol, and subject identifier.

The Department of Radiology at the NIC has its own Information and Technology (IT) dedicated staff under the leadership of Paul Lamonica who oversee the networking and security of the imaging data received. A dedicated file system on the ftp server is used to store and disseminate data. Imaging data is transferred via a secure tunnel from St. Jude's to our dedicated server. Imaging studies are backed up onto the NIC server, research computing share drive and backed daily by the Research Computing at Boston Children's Hospital under the supervision of Ryan Callahan.

Section VII
PBTC NIC Manual of Operations
PBTC NIC
Data Management System

VII. PBTC NIC Data Management System

The Clinical Research Information Technology Core will be used as a central location for data processing and management. Boston Children's Hospital, with collaboration from a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the Clinical Research Center. The iterative development and testing process results in a well-planned data collection strategy for individual studies. REDCap servers are housed in a local data center at Children's and all web-based information transmission is encrypted. REDCap has been disseminated for use locally at other institutions and currently supports > 230 academic/non-profit consortium partners on six continents and 24,000 research end-users (www.project-redcap.org)

The PBTC NIC Clinical Data Management System “Users Manual” diagrammatic flow chart, and protocol matrix follows.

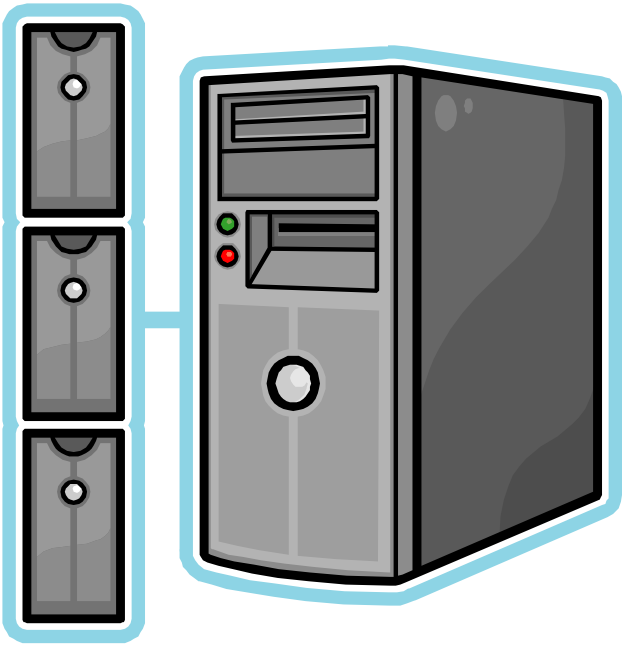
Clinical Data Management System

Users Manual

Project: Pediatric Brain Tumor Consortium

Neuroimaging Center

PI: Tina Young Poussaint, MD



Scientific Research Information System
Informatics Team, Clinical Research Program
Boston Children's Hospital,

Data Management System (User Manual)

Introduction

A Data Management System (DMS) is a software program of varying size and sophistication by which data collected on case report forms are stored, tracked and prepared for analysis. The data management system for this study is Web accessible and supports the following features.

- Basic Security (user authentication and authorization)
- Data Capture
    - Real-Time Validations
    - Outlier Identification
    - Read-Only Access
- Protocol Tracking
    - Custom Data Management Reports
- Audit Trails

This data management system is programmed to adhere to the operations of the study protocol (See pages 20 & 21). Clinical staff may use the DMS to track the progress and state of each case report form for each study participant. Standard data management reports will be added to the system to facilitate preparation of data for analysis.
Many of the features outlined above are described in detail in this manual. Further questions regarding DMS functionality should be directed to the clinical research specialist liaison of the Clinical Research Center office.

System Overview

Requirements

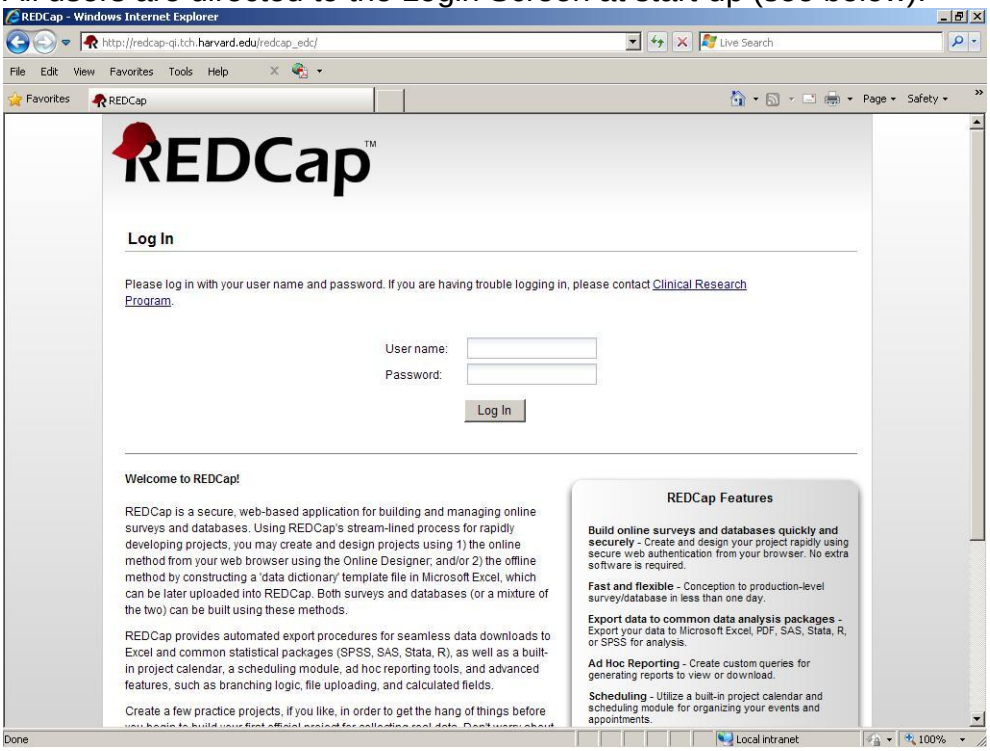
As stated previously, the DMS is a Web-based system accessible from inside the Boston Children's Hospital, intranet only. The Web site requires users to employ Internet Explorer version 8 or higher.
The data management system is accessible through the following URL.
http://redcap-qi.tch.harvard.edu/redcap_edc/

Application Security

CRC provides user access to key personnel for initial website access. Once access is granted, users will use their Children's ID and password to log in. User access to the database is determined by individual role on project.

Login Screen

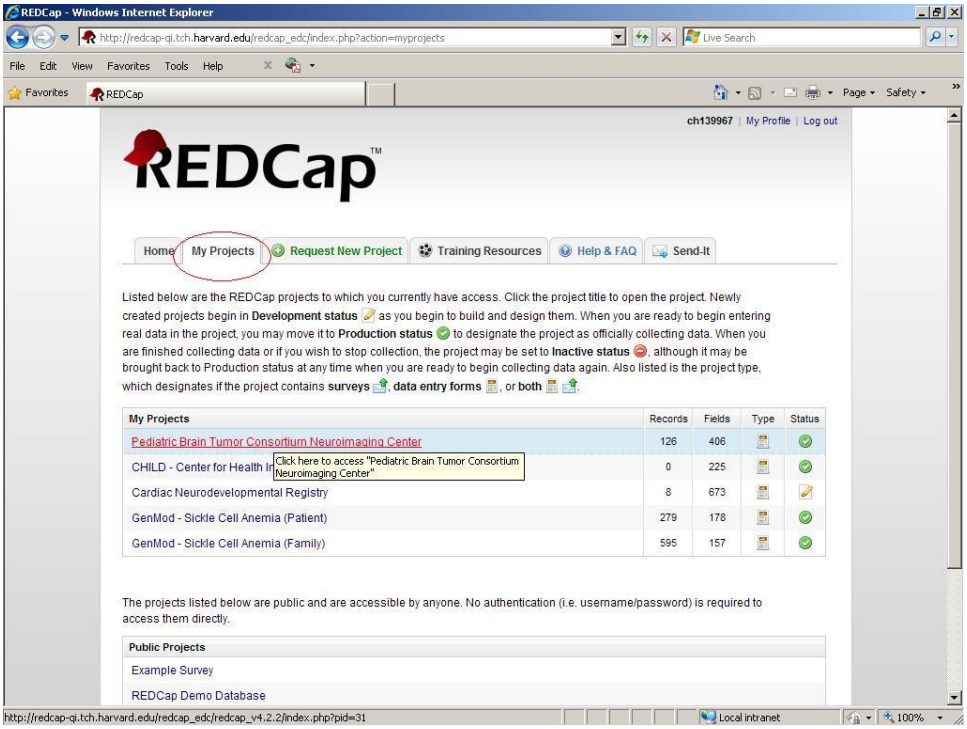
All users are directed to the Login Screen at start-up (see below).



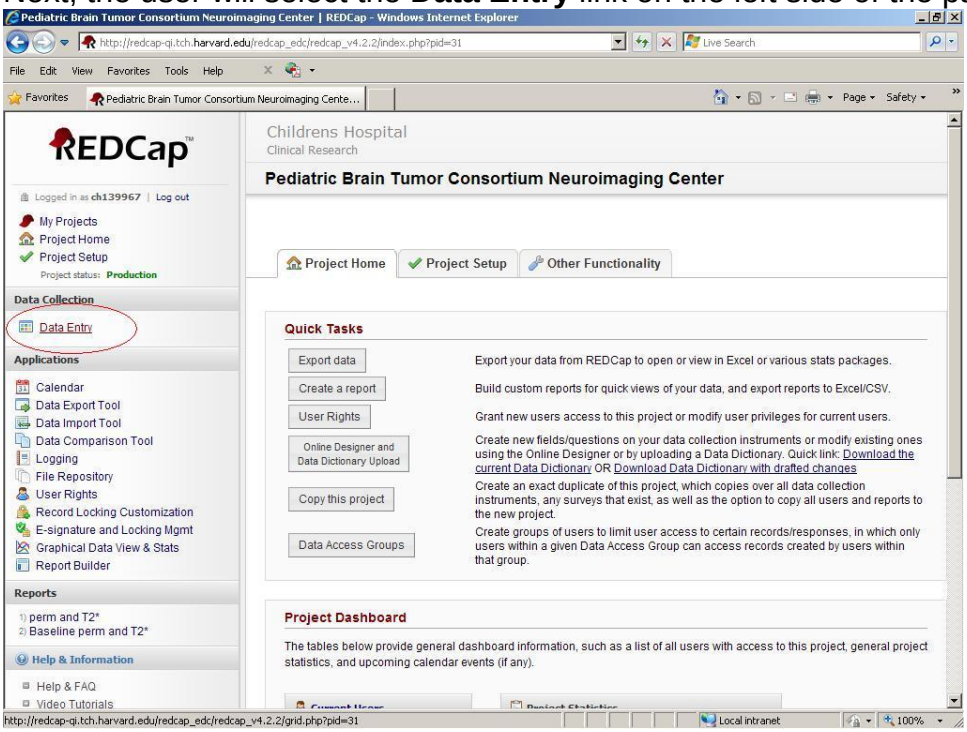
If a user has difficulty logging in, they may select the Clinical Research Center link and request help.

Home (Portal) Screen

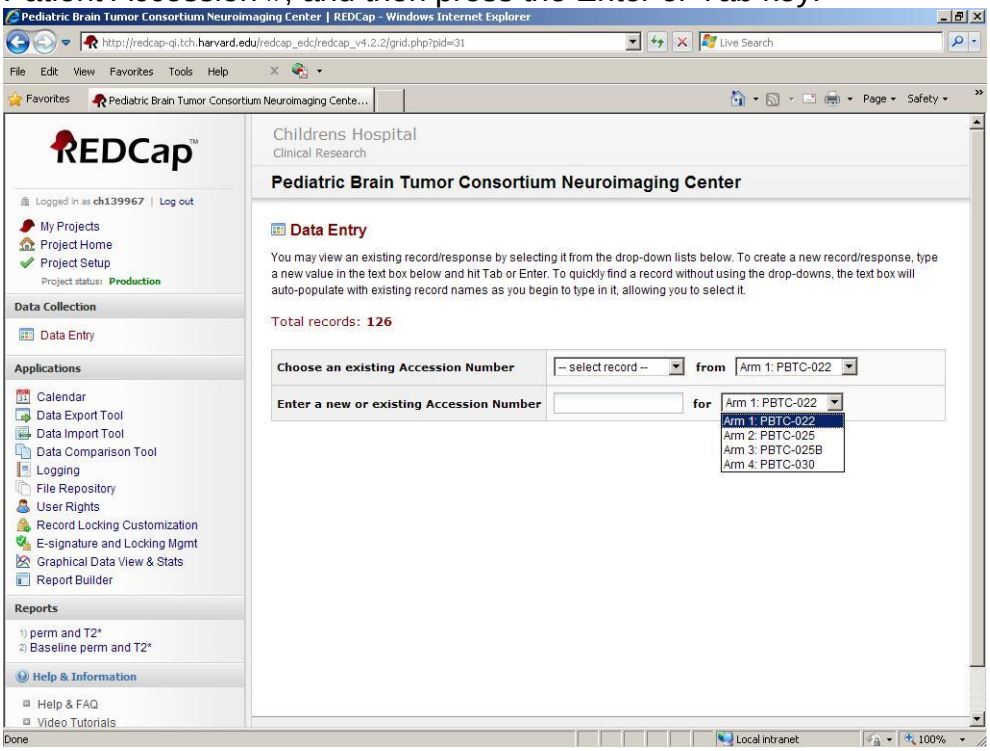
Upon logging in, the user must select the **My Projects** tab. From there, the user will click on the link labeled **Pediatric Brain Tumor Consortium Neuroimaging Center**.



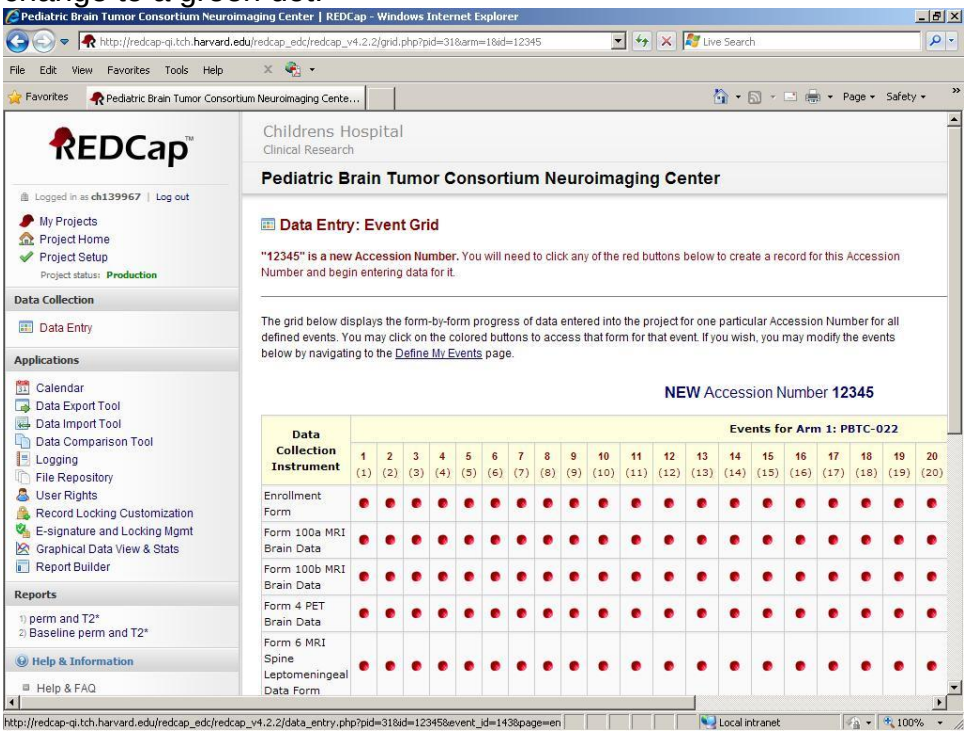
Next, the user will select the **Data Entry** link on the left side of the page.



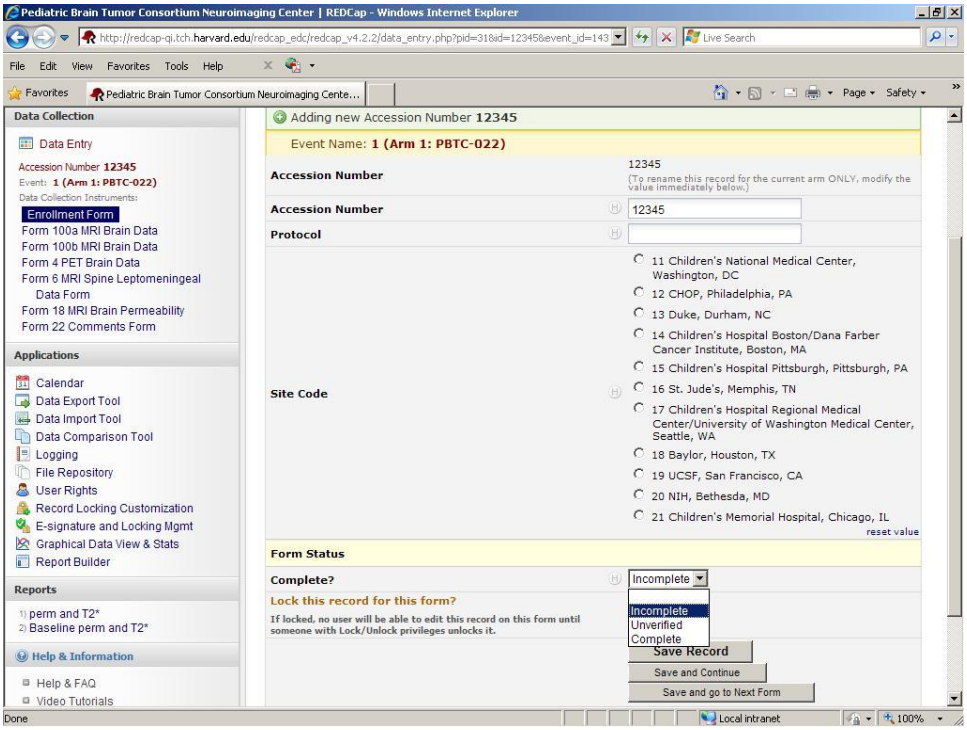
On the next screen, the user must select the arm (or PBTC Protocol), enter the Patient Accession #, and then press the Enter or Tab key.



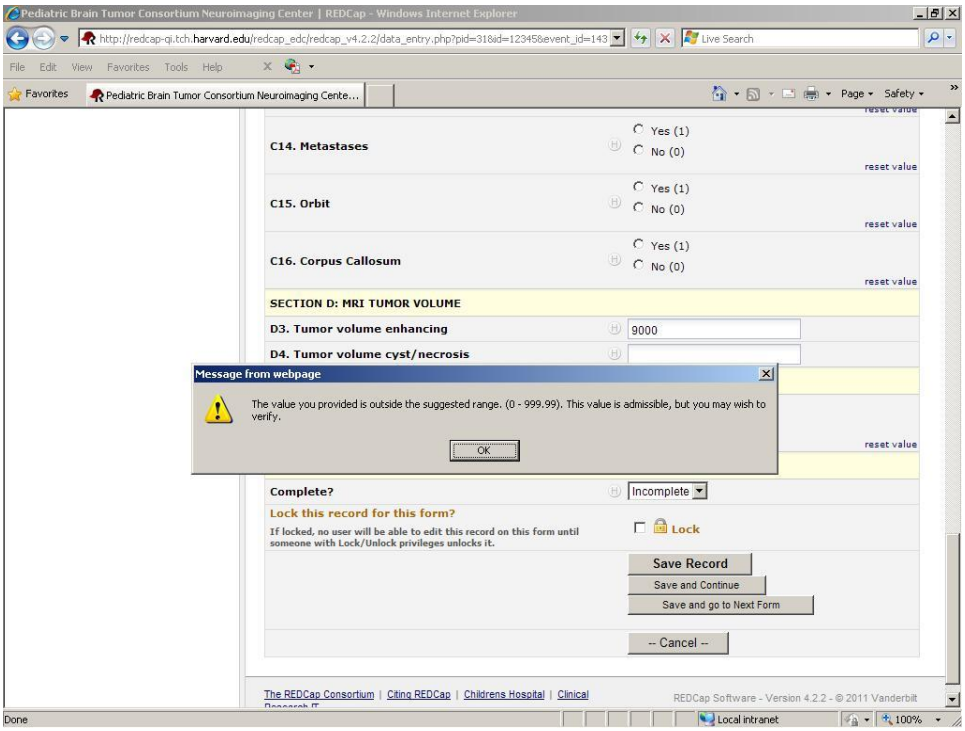
Next, the user must select the appropriate **Data Collection Instrument** (or Form) and **Event** Number for data entry. Red dots designate forms that have not been entered yet. Once a form has been entered and saved, the red dot will change to a green dot.



On the next screen, the user will be able to enter the data for the selected **Data Collection Instrument** (or Form) and **Event** Number. Once the form is entered, the user can specify whether the form is **Complete**, **Incomplete**, or **Unverified** and then click the **Save Record** button.



If an entered value is outside the specified range, a warning message will appear. The user will have the opportunity to accept or re-enter the out-of-range value.



Section VIII
PBTC NIC Manual of Operations
Quality Control Approaches

VIII. Quality Control Approaches

A. Training and Certification Requirements of the Neuroradiologist

The neuroradiologists at each site must be a Board certified radiologist with expertise in neuroimaging and/or CAQ accreditation**.**

B. Manuals of Operation

The NIC Manual of Operations documents all procedures or standard clinical protocols and research protocols, which address diagnostic standard protocols; intravenous contrast doses and infusion times when appropriate; image data storage; image data transfer; tumor volumetric analysis. Manuals are provided to each site for implementation of all imaging protocols and updated by the NIC throughout the study as appropriate.

C. Coordination and Communication

The NIC coordinates regular communication and meetings among the participating neuroradiologists of the Neuroimaging Committee and PET investigators of the PET Investigator Committee. This includes at least quarterly conference calls and biannual meetings as well as regular e-mail exchange for routine correspondence and questions. Dedicated consensus conferences and/or neuroradiology symposia for PET and MR investigators are held on a biannual basis at Boston Children's Hospital or PBTC meetings.

D. Site Visits

The NIC will conduct site visits as needed to each site to review procedures and compliance with all PBTC protocols. During the visit, participating sites will be expected to provide materials and answer questions directed by the NIC. An evaluation checklist will be completed at these site visits for inclusion in a Site Visit Report to the Principal Investigator and PBTC Steering Committees (see Site Visit Monitoring Report attached).

E. Reader Reliability

The reproducibility of the central image interpretation is evaluated by selecting a random 20% subsample of exams from each protocol for repeat interpretation at the NIC. All NIC neuroradiologists are blinded to the exams. Inter-rater and Intra-rater reliability is assessed by examining the percent agreement with the first reading (see Form 1b).

F. Data Quality

Regular meetings of the NIC staff occur with each download where images from the participating institutions are reviewed for routine compliance with the standardized imaging protocols set by the NIC. These data are entered into a web-based from at the OBC. NIC staff assess the diagnostic image quality and data integrity prior to submitting the CT, MR and PET data for analysis. Dr. Mulkern reviews the current QA protocols at each of the participating institutions including MR and MRS phantom controls in use. Compliance is insured with the QA protocols throughout the course of the study. In addition, the NIC, with the OBC, generates summary statistics and a report on the image quality and compliance with PBTC protocols by site and overall. These are distributed to the NC and Steering Committee for review on a biannual basis. An overview of the quality control procedures for each imaging study are as follows.

MRI Quality Control: Each site should have an American College of Radiology (ACR) phantom, which can be purchased (J.M. Specialty Parts, 11689 Sorrento Valley Rd, San Diego, CA 92121, 858-794-7200). This phantom comes equipped with a guide to performing specific tests of geometric accuracy, high contrast spatial resolution, slice thickness accuracy, slice position accuracy, image intensity uniformity, percent signal ghosting, and low contrast detectability. Each scanner used for the trial, scans the ACR phantom quarterly. These QC data sets are sent to the NIC on a regular basis where they are evaluated according to the recommendations of the ACR accreditation manual. Site scanner equipment includes Siemens, Phillips and GE scanners. A video for the MR QC process is posted on the website of the NIC: www.childrenshospital.org/research/pbtcnic Statistical data from the QA program is generated in the form of reports on an ongoing basis.

PET Quality Control: The quality control program for PET assures proper operation of all of the detector blocks and the accuracy of quantitation. Daily "blank" scans should be acquired to evaluate the operation of the detector blocks. Scanners provided by certain vendors require periodic updating of photomultiplier tubes to ensure proper operation. For General Electric scanners, an "update gains" check of the photomultiplier tubes should be performed weekly. For Siemens scanners, a "bucket setup" should be performed quarterly. Philips scanners do not require such a check. Modern PET scanners consist of thousands of small detectors and it is imperative for proper operation that their response be "normalized." Such normalization of the scanner should be performed quarterly according to the manufacturers' specifications. After normalization, a calibration must be performed for the scanner to be able to report the in vivo radiopharmaceutical distribution in Bq/mL or µCi/mL. Therefore, this calibration should be performed quarterly. PET scanners are complicated devices that require regular, preventive maintenance. Such preventive maintenance should be performed quarterly.

All members of the PBTC provide quarterly reports with regards to compliance to the PET quality control program described above. These reports require completing Form 5 (PET Quality Assurance Data Form) and sending it to

the Neuroimaging Center. Each site completes a one-time analysis of a PET phantom (Form 15). Statistical data from the PET QA program is generated in the form of reports on an ongoing basis.

The PBTC NIC was involved in a project with Paul Kinahan, PhD, of the University of Washington and Laurence Clarke, PhD of the NIH, that entails the imaging of a 20 cm cylindrical phantom with “hot” (i.e., higher activity concentration than the background) and “cold” (i.e., lower activity concentration than the background) features. This collaborative project, jointly overseen by the *Society of Nuclear Medicine* (SNM) and the *American Association of Physicists in Medicine* (AAPM), centered on the design of a phantom made with an equilibrium mixture of 68Ge/68Ga and equipped with 4 hot features of varying size (8-25 cm) and 3 cold features (all 25 cm of different materials) incorporated into a lid that can be used with the phantom imaged in 2005.

Following an initial evaluation of the phantom and corresponding, standardized imaging protocol and reporting form, the phantom was deployed to the respective PET imaging programs of the 10 PBTC NIC sites. We asked each site to 1) image the phantom as if it were a PBTC subject; 2) report which features were visible; and 3) record the SUV values for the background as well as the 4 hot features. The data obtained from this QC procedure enabled the NIC to better understand how quantitation differed among the PBTC sites and how limits of accuracy may varied depending on which clinical application was being tested. This study was published by the Journal of Medical Physics (Fahey FH, Kinahan PE, Doot RK, Kocak M, Thurston H, Poussaint TY. Variability in PET Quantitation Within a Multicenter Consortium. Med. Phys. 2010 Jul:37(7):3660-3666).

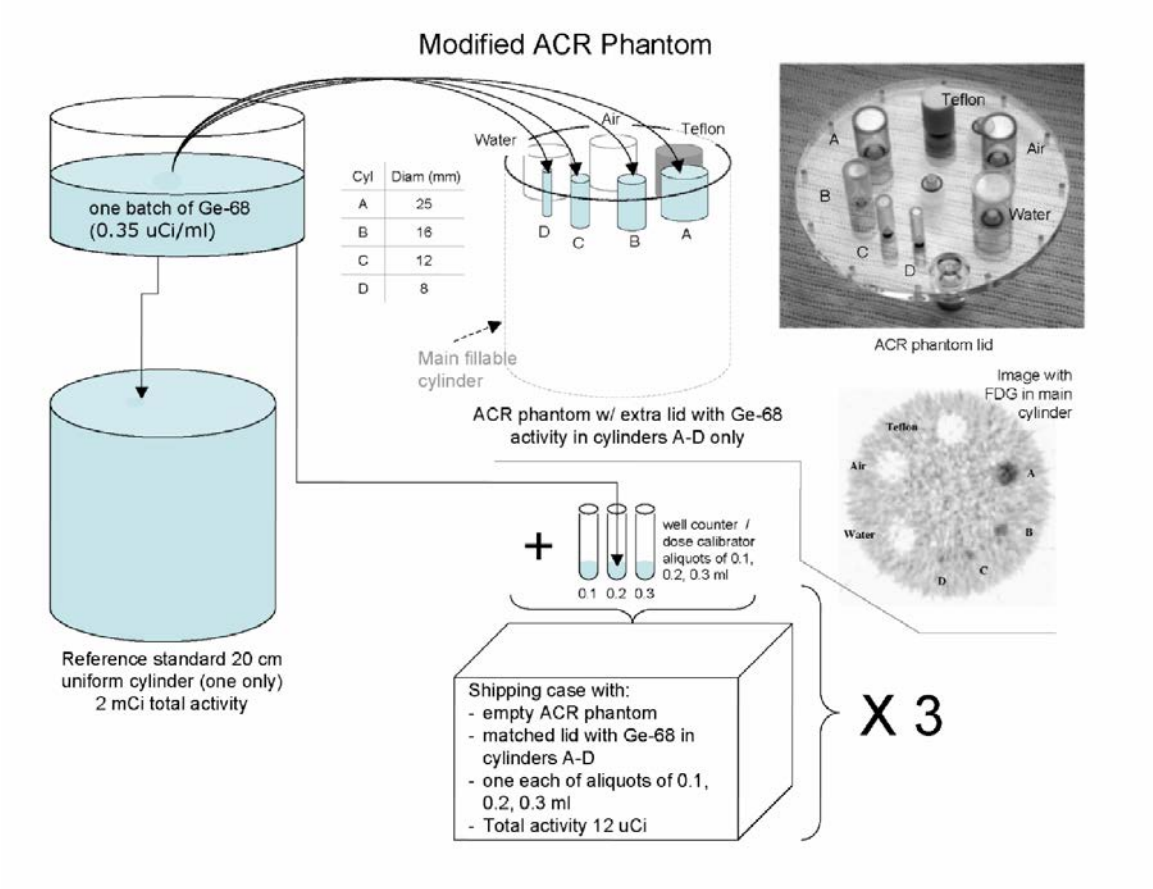


*Image courtesy of University of Washington – Seattle

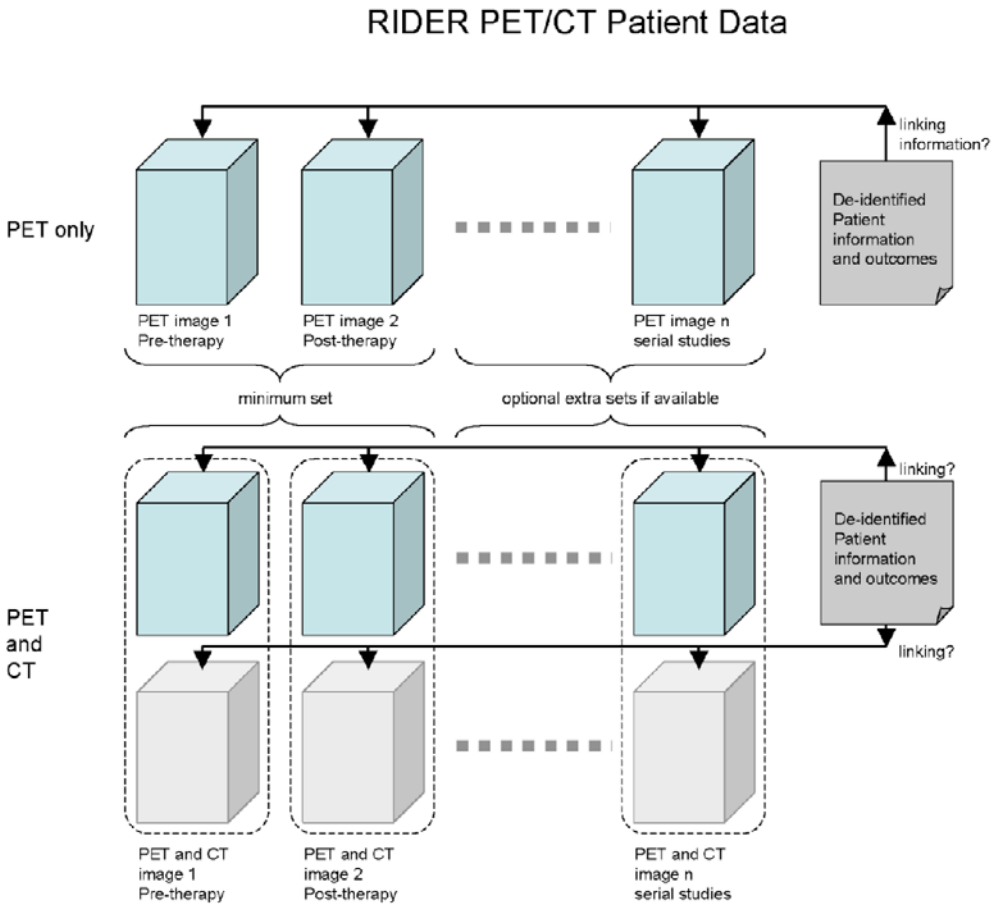


*Image courtesy of University of Washington – Seattle

PET Data Analysis:

All PET imaging data acquired via a PBTC protocol is forwarded to the OBC and subsequently sent to the NIC for analysis by download or FTP.

All PET imaging data, along with their corresponding MR data, are uploaded to a multi-modality processing and review station (Hermes Medical Systems). Whether the imaging data is present and readable is determined and noted on Form 4. If the data are not readable, a reason is given on Form 4. If readable, the PET data are registered to the MR and are subjectively reviewed in conjunction with the MR. A representative image transverse image plane through the tumor is selected for review. Uptake in the tumor (as defined by the MR) is subjectively judged on a 5-point scale (FDG less than white matter, FDG uptake similar to white matter, FDG uptake more than white matter but less than gray matter, FDG uptake similar to gray matter, FDG uptake greater than gray matter) The uniformity of the uptake is judged to be 0-25%, 26-50%, 51-75% or 76-100% of the tumor as defined by MR. It is also determined whether the FDG uptake correlates with regions of MRI contrast enhancement. This subjective analysis is followed by quantitative, region of interest (ROI) analyses. On the

representative transverse plane selected above, 4 ROIs are drawn: one around the tumor, one in comparable gray matter, one in comparable white matter and one about the entire brain. If the tumor is not in a transverse slice that contains comparable gray and white matter, a second transverse plane is selected for the comparison ROIs. The mean and maximum pixel values within each of the ROIs are recorded. Ratios of tumor/gray matter, tumor/white matter and tumor/whole brain using both mean and maximum pixel counts are determined.

3D Image Analysis

In selected cases 3D image analysis has been done. 3D Image Analysis Tumor volumes of interest (VOIs) are defined on both FLAIR and T1 post-contrast (PC) MR images. The areas defined are the areas of hyperintense signal on the FLAIR images and enhancing tumor on the T1 post-contrast MR images. After volumes of interest are manually drawn on the MR images, they are confirmed by a nuclear medicine physicist and pediatric neuroradiologist and transferred to the co-registered PET images. Four 3D FDG uptake metrics have been determined for each PET VOI. The mean pixel value within the VOI is determined and this value is normalized by the mean value within the comparison VOI of either normal gray or white matter yielding the Tumor Gray Matter Ratio (Mean) and Tumor White Matter Ratio (Mean) values, respectively. The Tumor Gray Matter Ratio (Maximum) and Tumor White Matter ratio (Maximum) is defined similarly except the maximum pixel value within the VOI is used instead of the mean. For the Tumor Gray matter Ratio (Total) and the Tumor White Matter Ratio (Total), all of the pixel values within the VOI are added yielding a cumulative metric, and this value is normalized by a similar value for the gray or matter comparison VOI, respectively. The inhomogeneity index is defined as the ratio of the standard deviation of the pixel values within the VOI normalized by the mean.

Section IX
PBTC NIC Manual of Operations
Appendices, Protocols and Forms

IX. APPENDICES OF NEUROIMAGING STUDIES PROTOCOLS AND FORMS

APPENDIX A: PBTC NIC MR PROTOCOLS OF BRAIN AND SPINE

A1. PBTC MR Protocol Brain

0) Localizer of Choice

Note: Efforts should be made to have same slice locations and thicknesses for sequences 2, 3 and 5.

1) Axial T1-weighted spin echo (SE) whole head, TR/TE = (500-700)/minimum full, receiver bandwidth (RB) = ± 16 kHz, FOV = 18-24 cm, slice thickness/gap = 4/0 (mm), NEX = 2, no phase wrap option, matrix = 256 x 192 (frequency x phase), frequency direction = A/P

1*) For hemorrhage: Axial 2D gradient echo sequence whole head: TR/TE/FA = (500-700)/25/90, 256x192 (frequency x phase), FOV = 18-24 cm, slice thickness/gap = 5/0, NEX = 2, frequency directions = A/P

2) Axial T2-weighted fast spin echo (FSE), TR/ETE = (4000-6000)/80-100, ETL = 10-16, RB = ± 16 kHz, FOV = 18-24 cm, slice thickness/gap = 4/0 interleaved, NEX = 2, matrix = 256 x 192, flow compensation option, frequency direction A/P

2a) 3T optional replacement) Axial 3D Fast Spin Echo sequence with variable flip angle (GE XETA sequence, Siemens SPACE sequence). ETL = 65, parallel imaging acceleration = 2, TR = 3 s, Effective TE = 80 ms, 200 slices, 1 mm thickness, 6 minute scan times

3) Axial FLAIR, TR/TI/ETE = 10,000/2200/162, ETL = 16, RB = ± 32 kHz, FOV = 18-24 cm, slice thickness/gap = 4/0 mm, NEX = 1, flow comp, frequency direction A/P

4a) Perfusion –T2* Gradient Echo Technique
Perfusion scan axial echo planar imaging, gradient echo mode, single shot, (reduced coverage 10 slices only), receiver bandwidth = ± 64 kHz, matrix = 128 x 128, TR/TE = 1500/45-60), slice thickness/gap = 6/3 for supratentorial mass, 3/0 for brainstem mass, FOV = 18-24 cm, NEX = 1, frequency direction R/L, 45 to 60 phases, 10 phases prior to bolus injection of GdDTPA, frequency direction R/L, flip angle=90. For child <10 kg, injection rate 1-2cc/sec; >10kg to <35kg, injection rate =2cc/sec; >35kg, injection rate =3 - 4 cc/sec, 22G IV minimum.

4b) MR permeability consists of dynamic T1-weighted 3D SPGR (FLASH, FFE), minimum resolution 128x128x16, 24cm FOV, TR min, TE min, flip = 30 degrees, which is repeated 40 times (using multiphase/dynamics option).

The dose of Gadolinium DTPA (GdDTPA) is 0.1mmol/kg body weight and injected at a rate of 2ml/sec approximately 10 seconds after scanning starts (to collect 2-3 baseline image sets). Kinetic modeling of the dynamic signal changes yields estimates of regional fractional blood volume and microvascular permeability (Ktrans), a sensitive indicator of blood brain disruption and a putative correlate of angiogenesis.

5) Axial T1-weighted spin echo (SE) post contrast whole brain, TR/TE = 500-700/minimum full, receiver bandwidth = $\pm$ 16 kHz, FOV = 18-24 cm, slice thickness/gap = 4/0 (interleaved acquisitions), NEX = 2, frequency direction = A/P, matrix = 256 x 192

6) PROBE-P, PRESS single voxel spectroscopy, TR/TE = 1500/144, FOV = 24 cm, voxel size = 15 x 1 x 1 cm3 (approximately) positioned in solid tumor using post-GD T1, FLAIR and T2 images, total scans = 128

7) Diffusion imaging, single-shot echo planar spin echo, TR/TE = 2000/80, matrix = 128 x 128, b-factor = 5/1000 s/mm^2, one baseline plus 6 diffusion sensitization directions for diffusion tensor and trace imaging, receiver bandwidth = $\pm$ 64 kHz, frequency direction = R/L, slice thickness/gap = 5 or 6/0 whole brain, decrease thickness for brainstem tumors.

8a) Diffusion Tensor Imaging Protocol: GE DTI protocol for 1.5T machines:
DWI-EPI with ASSET(no fat sat)(with pure calibration)
Image options: EPI, DIFF ASSET-2.00 Ph, #shots1
matrix size 96x96x50 (50 is the number of slices)
TE: min
NEX: 1
Number of baselines: 6
Phase FV: 1(full)
Shim Auto
Scan direction: Axial IS
Bandwidth: 62.5 Spatial resolution: 2.5 mm by 2.5 mm by 2.5 mm
TR: < 10 seconds – Can increase TR up to 12-13 seconds.
FOV: 24
Freq: R/L
Phase correction
b-value: 1000
directions: 30
Select ASSET-2.00ph and PURE user CVs(control variables): CV6-CV0.00
Other diffusion options: recon all images

8b) Diffusion Tensor Imaging Protocol: Siemens DTI protocol for 1.5T machines:
DWI-EPI
Mode = MDDW
Number of B values: 2
b=0 and b=1000
directions: 30
Number of baselines: (problematic on SIEMENS)
matrix size 96x96x50
Spatial resolution: 2.5 mm by 2.5 mm by 2.5 mm
Slice thickness: 2.5 mm
Base resolution: 96x96
Phase resolution: 100%
Number of averages: 1
FOV: 240mm
Phase FOV: 100%
Shim Auto
Scan direction: Axial
Bandwidth: 1302 Hz/Px
TR: < 10 seconds
TE: min (as low as allowed)
Freq: R/L Phase correction
Fat sat: off GRAPPA = 2
Diffusion recon options: Tensor checkbox should also be checked (but make sure your PACS system can manage these tensor recon files, otherwise just send them to PBTC if your PACS cannot handle them)

A2. Intra-Tumoral Hemorrhage (ITH)

1.) Neuroimaging Definition of Intratumoral Hemorrhage (ITH):

The PBTC neuroimaging committee has developed the following definition for ITH: Acute or subacute hemorrhage based on T1, T2 and gradient echo images that are greater than punctate in extent. Evidence of chronic blood products alone or punctate hemorrhage will not be considered an ITH for purposes of the stopping rule. (Note: any evidence of ITH, including old blood or punctate hemorrhage, prior to beginning treatment would make the patient ineligible).

2.) Definition of Symptomatic ITH:

A symptomatic ITH is defined as: neurologically significant events temporally related to an MRI demonstrating ITH, in which either:

i. Patients with grade 2 or less neurologic dysfunction at baseline have an increase to grade 3 or 4 dysfunction, OR
ii. Patients with grade 3 dysfunction have an increase to grade 4.

3.) ITH and Stopping Rule

The following ITH occurrences will apply to the stopping rule unless the attribution is definitely not related to the drug (e.g., definite disease progression with associated ITH may be attributed to disease rather than to the investigational agent).

i. Patients with symptomatic ITH
ii. Asymptomatic hemorrhage will not require that the patient be removed from study, or count during the stopping rule unless hemorrhage is progressive. MRI must be repeated 2 weeks following scan demonstrating asymptomatic hemorrhage. If there is evidence of new hemorrhage, the patient will be removed from study and the event will count towards the stopping rule.

A3. PBTC NIC MR Protocol Spine

For leptomeningeal seeding:

1) Sagittal T1-weighted spin echo, TR/TE = 400/minimum full, FOV = 24 cm can increase to 48 cm with 0.75 partial FOV option, thickness/gap = 3/0 mm, spatial sat A/P, NEX = 2, frequency direction = S/I, receiver bandwidth = $\pm$ 16 kHz, matrix = 192 x 256, can increase to 384 x 512

2) PRN Axial T1-weighted spin-echo, TR/TE = 600/minimum full, FOV = 16 cm, thickness/gap = 4/1, NEX = 2, frequency direction R/L, matrix = 256 x 224, receiver bandwidth = $\pm$ 16 kHz

If concern about spinal cord damage/injury:

1) Axial T2-weighted FSE, TR/ETE/ETL = 4000/85/12, FOV = 16 cm with 0.75 partial FOV option, thickness/gap = 4/1 mm, frequency direction R/L, NEX = 2, matrix = 256 x 256, receiver bandwidth = $\pm$ 16 kHz, flow comp option, FSE-XL if available

2) Sagittal T2-weighted FSE, TR/ETE/ETL = 4000/85/12, FOV = 24 cm with 0.75 partial FOV option, thickness/gap = 3/0 mm, spatial sat S/I, NEX = 2, matrix = 256 x 256, flow comp option, FSE-XL if available

A4. Data Form Completion and Entry

All images are read by the NIC neuroradiologists. The NIC neuroradiologist completes the PBTC MRI compliance and data form for the brain and spine, and the forms are provided to Audrey Gill at the Clinical Research Center for data entry through the PBTC web-based data management system. These data are managed centrally for statistical analysis by the PBTC OBC.

A5. Questions

For any questions regarding the MR Protocol of the Brain or Spine, sites should contact Robert Mulkern, Ph.D., 617-355-3737, email: rmulkern@yahoo.com.

APPENDIX B: PBTC NIC MRI QUALITY ASSURANCE PROCEDURES

A complete report of the current state of MRI QC with quantitative listings of the results from each site is compiled and a running update of the overall QC report is handled by the Clinical Research Center at Boston Children's Hospital. Dr. Mulkern receives the completed forms from each site as they perform quarterly (at minimum) tests. He archives the hard copy, performs a close inspection of each report to identify errors or outliers in the form; then the new data is entered by the CRC into the QC report. Data and statistics associated with each of the seven tests for each site are maintained. Regular meetings (monthly or more) between Dr. Mulkern and the CRC personnel have been established to maintain an active QC MRI program. Sites will be notified when action level values exceeding 15% of the mean for any measurement are noted by the NIC. Each site should follow its own institutional procedures in assessing and/or repairing the scanner in question.

Sites should also have a spectroscopy phantom as supplied by their manufacturer. In the case of General Electric sites, the phantom is referred to as the Braino phantom as it contains concentrations of the major metabolites similar to that found in the human brain. At least quarterly, this phantom should be scanned and the values for the three resonances NAA, Cho and Cr associated ratios should be recorded in the PBTC QA form

The primary quality control testing should be done quarterly using the American College of Radiology (ACR) MRI test phantom which is also used for the accreditation process of MRI systems. Each site should purchase the phantom which comes with manuals on how to scan and analyze the subsequent data. For ACR phantom purchase, please contact:

J.M. Specialty Parts
11689-Q Sorrento Valley Rd.
San Diego, CA 92121
858 794-7200

B1. Typical Report:

The ACR phantom was imaged according to the guidelines of the ACR pamphlet "Site scanning instructions for use of the MR phantom" and subsequent measurements were made from sagittal and axial images acquired with T1-weighted and T2-weighted spin echo sequences.

B2. Test Procedure

Seven specific tests are performed from a scanning session that should last less than 20 minutes. A description of each exam and analysis as performed here at Boston Children's Hospital is provided below. Note that all 7 tests provided results which were within the acceptable limits of image quality specified by the ACR which will also be used as the PBTC criteria for acceptable scanning.

Test 1: Geometric Accuracy

Linear measurements of the dimensions of the phantom along several directions are made and compared with known dimensions of the phantom. Measured values must be within ± 2 mm of known dimensions.

Results:

a) end-to-end-sagittal view, localizer slice, measured value = 147 mm, actual value = 148 mm.
b) top-to-bottom axial view, slice 1, measured value = 189 mm, actual value = 190 mm
c) left-to-right axial view, slice 1, measured value = 189 mm, actual value = 190 mm
d) top-to-bottom axial view, slice 7, measured value = 190 mm, actual value = 190 mm
e) left-to-right axial view, slice 7, measured value = 190 mm, actual value = 190 mm
f) diagonal 1, axial view, slice 7, measured value = 190 mm, actual value = 190 mm
g) diagonal 2, axial view, slice 7, measured value = 189 mm, actual value = 190mm

Test 2: High Contrast Spatial Resolution

Three pairs of 4 x 4 arrays of 1.1 mm, 1.0 mm and 0.9 mm holes are imaged and counted with imaging sequences having a 1 mm spatial resolution specification. The number of distinguishable holes in each array are identified.

Array 1 (1.1 mm holes) – all holes identified
Array 2 (1.0 mm holes) – all holes identified
Array 3 (0.9 mm holes) – only ¼ holes identified

Test 3: Slice Thickness Accuracy

The slice thickness insert of the phantom consists of two crossed ramps which yield estimates of the actual vs. proscribed slice thickness of 5 mm. Length measurements of the top and bottom ramp signal intensities were 63 mm and 41

mm respectively from which the actual slice thickness is calculated using the formula

Slice thickness = 0.2 x (63 x 41/(63 + 41)) = 4.97 mm

Which is well within the specified range of 5.0 $\pm$ 0.7 mm required for acceptance.

Test 4: Slice Position Accuracy

Slices 1 and 11 are aligned with the vertices of crossed 45º wedges so that when perfectly aligned, two black bars will appear next to each other in each of the images of slice 1 and 11. For perfect slice position, the bars will have equal length. If the difference between the bar lengths is less than 5 mm, then the center of the slices are within 2.5 mm of the prescribed locations and within tolerance. The bar length differences in slices 1 and 11 were approximately 3 mm, well within tolerance (less than 5 mm) for this measurement.

Test 5: Image Intensity Uniformity

A uniform region of the phantom (axial slice 7, 19,849 mm^2 area) was selected and two regions-of-interest (ROI's), 100 mm^2 each, with the highest and lowest signal intensities were identified. Signal intensities from these two ROI's were used to calculate the percent integral uniformity (PUI) through the equation

$$PUI = 100 \times (1 - (ROI_{high} - ROI_{low})/(ROI_{high} + ROI_{low}))$$

The ROI_{high} and ROI_{low} were measured as 1374 and 1227, respectively, yielding a PUI value of 94 %. This is above the minimum PUI value of 87.5 % required for acceptance.

Test 6: Percent Signal Ghosting

The large ROI identified for image intensity uniformity (Test 5) is used to estimate signal intensity within the ACR phantom (ROI_{large}). Four additional measurements are made in the air outside of the phantom to estimate noise values along both the frequency and phase encode dimensions. Ghost signal occurs only along the phase encoding direction so that the ghost signal is calculated as

$$\text{Ghosting ratio} = (\text{left} + \text{right} - \text{top} - \text{bottom})/(2 \times ROI_{large})$$

Measurements were 1321, 11.1, 10.9, 17.8 and 16.8 for the large, top, bottom, left and right ROI's respectively where the left and right were the phase encode noise measurements containing the ghost signals. The ghosting ratio was thus calculated as 0.005 which is well below the 0.025 limit specified for acceptance.

Test 7: Low Contrast Object Detectability

Slices 8 – 11 of the ACR phantom contain 10 spokes each containing 3 low contrast objects per spoke with contrast decreasing from 5.1 %, 3.6 %, 2.5 % and 1.4 % for slices 11 – 8, respectively. One counts the number of spokes for which all three objects can be seen in each slice and sums the number of spokes so-counted through all four slices (a spoke is not counted if any one of the three objects are not visualized). From the T1 spin echo scans, 36 spokes were counted and for the T2-weighted spin-echo sequence 37 spokes were counted. This far exceeds the 9 spokes required per scan for acceptance.

B3. Data Form Completion and Entry

Sites should complete the PBTC MRI QUALITY ASSURANCE DATA FORM - FORM #2 each time the phantom is scanned and fax the form to Audrey Gill, Research Coordinator, at Boston Children's Hospital (fax #617-730-0828).

B4. Reporting and Follow-up

Sites will be notified when action level values exceeding 15 % of the mean for any measurement are noted by the NIC. Each site should follow its own institutional procedures in assessing and/or repairing the scanner in question.

B5. Questions

For any questions regarding the implementation of the quality assurance procedures, sites should contact: Robert Mulkern, Ph.D. at 617-355-3737, email: rmulkern@yahoo.com

APPENDIX C: PBTC NIC PET FACILITY PROCEDURES

GE ADVANCE

C1. NEURO: FDG Brain Tumor Protocol

Patient Prep: Adult- NPO for 4 hours prior to F-18 FDG injection (water encouraged).

Infant- NPO for 2 hours prior to F-18 FDG injection (water encouraged). I.V. or hep lock is necessary along with a possible sedation order.

Radiopharmaceutical: F-18 FDG

Dose: Determined by patient weight with minimum and maximum values.

Adult- 5 - 15 mCi
Pediatric- 0.5-10.0 mCi (0.143 mCi/kg)

Acquisition mode: 3D

Acquisition time: 6 mins

Attenuation correction: Performed using either a calculated method, a measured method with 3 min transmission scan with segmentation applied or CT if the study is acquired on a PET/CT scanner.

C2. Method

1) Patient is interviewed for pertinent medical history and discussion of PET procedure.
2) Injection of F-18 FDg is made with the patient in supine position. After the injection the room lights are dimmed. The patient is instructed to stay awake but quiet. Approximately 80% of the glucose localization occurs in 20 minutes, so movement and/or sedation may proceed 20 minutes after injection.
3) Patient is asked to empty bladder after injection.
4) Imaging begins at 40-60 minutes post F-18 FDG injection.
5) Patient is positioned in PET head holder.
6) Patient is asked to empty bladder post scanning; hydration and frequent bladder emptying are encouraged.
7) Any variation in the above technique should be brought to the attention of the PET attending physician.
8) **Any possibility of pregnancy and/or breastfeeding must be ruled out prior to injection/inhalation of radioactive material.**

C3. Data Form Completion and Entry

All images are read by the NIC PET nuclear medicine physician and physicist in conjunction with the NIC neuroradiologist. The NIC PET physician completes the PBTC PET compliance and data form and the form is provided to Rajna Filip-Dhima at the Clinical Research Center for data entry into the PBTC web-based data management system. These data are managed centrally by the PBTC Biostatistics and Operations Center.

C4. Questions

For any questions regarding the PET procedures, sites should contact Frederic Fahey at (617) 355-2809 or e-mail at frederic.fahey@childrens.harvard.edu.

Data for calculation of SUV, i.e. injected activity, time of injection, time of scan, patient weight and patient height as well as additional parameters (see PET support form 14) are recorded for each PET exam and uploaded with the study to the OBC.

APPENDIX D: PBTC NIC CASE REPORT FORMS

Form 100a	MRI Brain Data
Form 100b	MRI Brain Data
Form 2	MRI Quality Assurance
Form 3	Retired: No longer in use
Form 4	PET Brain Data
Form 5	PET Quality Assurance
Form 6	MRI Spine Data
Form 7	Retired: No longer in use
Form 8	Retired: No longer in use
Form 9a	MRI Brain Leptomeningeal Data
Form 10	Retired: No longer in use
Form 11	Retired: No longer in use
Form 12	Retired: No longer in use
Form 13	Retired: No longer in use
Form 14	PET Support Data
Form 15	PET Phantom Acquisition Form
Form 16	Merged: Now part of Form 1a
Form 17	Fusion Volumetrics
Form 18	MRI Brain Permeability
Form 19	Site Visit Mandatory Reporting Form
Form 20	^{68}Ge ACR Phantom Acquisition Form
Form 21	Spinal Tumor Volume
Form 22	Comments Form
Form 23	RECIST Measurements
Form 24	Macdonald Criteria
Form 25	Diffusion Tensor Imaging
Form 26	MR Contrast Survey
Form 27	ADC Histogram Analysis
Form 28	MRI Brain Permeability
Form 29	ADC Histogram Quality Assurance
Form 30	sFDM QA & Data Form