ACRIN 6667
SUMMARY OF CHANGES

October 9, 2003 Amendment #2

Participating Sites List
In the list of participating sites, at #11, University of Pennsylvania, Susan Weinstein has been added as a co-investigator.

#12 has been changed from Dr. Fenstermacher at MD Anderson to Dr. Schilling at Boca Raton Community Hospital.

Schema Page:
In the fifth sentence of the first paragraph, "60 days" has been changed to "90 days." Throughout the protocol, we have changed the text so that the MRI is now allowed within 90 days of the negative mammogram and CBE.

In the third bullet of the eligibility list, "60 days" has been changed to "90 days."

1.0
In the third sentence, "60 days" has been changed to "90 days."

3.1
In the second and third sentences of the second paragraph, "60 days" has been changed to "90 days."

4.0
The following has been added at the end of the third sentence: "for the diagnosis and 90 days prior to the MRI for the mammogram and CBE."

5.0
In the third paragraph, "60 days" has been changed to "90 days."

5.1.3
"60 days" has been changed to "90 days."

6.1
In the second section, "Parts 1 and 2" has been deleted. The third sentence has been changed from "faxed or mailed" to "emailed, faxed, or mailed." In the fourth sentence "sample images" has been changed to "sample patient images." The sixth and seventh sentences have been deleted. In the last sentence, "Dr. Connie Lehman at the University of Washington" has been changed to "ACRIN."

7.1.1
In the last sentence of this section, "one business day" has been changed to "two business days."

8.2.3
The following has been added at the end of the third sentence: ", using a pre-assigned reader ID when applicable."

8.6.2
Page 11: In the last sentence "Executive Committee" has been changed to "ACRIN Steering Committee" to reflect a change in ACRIN's committee structure.

8.6.4
In the row for the MRI Tracking Diagram (B2), "within 8 weeks of registration" has been changed to "*as needed*, site will be notified of addition to case calendar."

In the row for Biopsy Procedure Form (AB), the time of submission has been changed from "within 4 weeks of registration" to "As needed, within 4 weeks of biopsy/surgical procedure."

In the row for the Pathology Report (P1), "as needed" has been added to the time of submission. Below that row, two new rows have been added:

Surgical Report[c] **(S2)**	Clinical Site	ACR	As needed, within 4 weeks of biopsy/surgical procedure
Surgical Pathology Report[c] **(S5)**	Clinical Site	ACR	As needed, within 4 weeks of biopsy/surgical procedure

For the Re-Reader Mammogram Form (XC), the time of submission has been changed from "site will be notified of addition to the case calendar" to "per section 13.3."

9.1
The first two sentences originally read, "Institutional on-site audits will be completed within 18 months of a site's enrolling its first ACRIN participant. Subsequent audits will be scheduled per the outcome of the initial audit." Those sentences have been replaced by the following: "Institutions will be eligible for on-site audit as soon as they accrue 25 participants. If an audit is acceptable, a subsequent audit will be scheduled 12 months after the initial audit date. If an audit is unacceptable, a follow-up audit will be scheduled as per the ACRIN Audit Manual guidelines." In the following sentence, "Biomedical Imaging Program (BIP)" has been changed to "Cancer Imaging Program (CIP)."

9.2
In the first sentence, "the BDMC" was changed to "ACRIN staff."

9.5
In the first sentence, "Quality Assurance reviewer" has been changed to "Quality Control Committee."

9.6
After the second bullet, a new bullet has been added: "surgery reports or legible copies".

9.7
The Audit/Source Documentation Table has been extensively revised. The new table is below:

9.7 Audit/Source Documentation

Case Reporting Form	***Data Items***	***Source Documentation***
Eligibility Checklist ***(A0)*** *(Patient registration must occur within 2 business days of initial MRI scan)*	***Recent biopsy confirmed breast cancer***	*Path report (P1)***
	Negative or benign mammogram	*Mammogram report (I2)***
	Negative or benign CBE	*Hospital or clinic chart or legible copy of A0 form completed, signed, and dated by subject* ***and*** *signed and dated by RA*
	Treatment plan, treatment	
	Exclusion criteria	
Initial Evaluation Form ***(I1)***	***Patient history*** *(menopausal status, date of last period, # of full term pregnancies, age at menarche, age at menopause, breast implant, history of hormone use, history of prior biopsy in study breast)*	*Hospital or clinic chart or legible copy of I1 form completed, signed, and dated by subject* ***and*** *signed and dated by RA*
	Breast cancer diagnosis *(histology, date of diagnosis, laterality)*	*Path report* ***(P1)*****
Initial Mammogram Assessment Form ***(IA)***		*Mammogram Report* ***(I2)***** ***and*** *IA form*** completed, signed, and dated by RA* ***or*** *MD*
Ultrasound Form ***(IS)*** *as needed*		***Ultrasound Report*** *(DR)** and* ***IS form*** completed, signed, and dated by RA or MD***
Ultrasound Report ***(DR)***		*Ultrasound Report (DR) ***
Initial MRI Assessment Form ***(M3)*** *(Patient registration must occur within 2 business days of initial MRI scan)*		*MRI Report* ***(ME)***** *signed and dated by study MD* ***and*** *completed M3 form*** signed and dated by RA or MD* ***OR*** *MRI Report (ME)** signed and dated by non-study MD and completed M3 form*** signed and dated by study MD*
Biopsy Procedure Form ***(AB)*** *as needed*	*If biopsy, excision, mastectomy or other surgery is performed on contralateral (study) breast*	*Pathology Report* ***(P1)***** *as needed* ***and*** *Biopsy Procedure Form (AB)***, completed, signed, and dated by RA or MD*
Post-MRI Mammogram Assessment Form ***(IM)***		*Mammogram Report* ***(I2)***** ***and*** *IM form*** completed, signed, and dated by RA or MD*
MRI Short Interval Imaging Form ***(M4)***		*MRI Report* ***(ME)***** *signed and dated by study MD* ***and*** *completed M4 form*** signed and dated by RA or MD* ***OR*** *MRI Report (ME)** signed and dated by non-study MD and completed M4 form*** signed and dated by study MD*

Pathology Evaluation Form ***(PA, PD, PE)*** *as needed*	*If biopsy, excision, mastectomy or other surgery is performed on contralateral (study) breast*	*Pathology Report* ***(P1)*** ** *as needed PA, PD, and PE Forms completed, signed, and dated by RA or MD*
Protocol Variation Form ***(PR)***	*Reviewed for cases in which a variation has been found.*	*Completed, signed, and dated by RA*
F1 Follow-Up Assessment Form ***(F1)*** *To be collected 12 to 16 months after initial study MRI and 24-30 months after the initial study MRI**	*If CBE is performed on contralateral (study) breast 0-16* months following initial MRI*	*Hospital or clinic chart or legible copy of F1 form*** completed, signed, and dated by RA or MD*
	If Mammogram, Ultrasound, or MRI is performed on contralateral (study) breast 0-16 months following initial MRI*	*Mammogram Report* ***(I2)**** *Ultrasound Report* ***(DR)**** *MRI Report* ***(ME)**** *as needed* ***and*** *F1 Form*** completed, signed, and dated by RA or MD*
	If biopsy, excision, mastectomy or other surgery is performed on contralateral (study) breast 0-16 months following initial MRI*	*Pathology Report* ***(P1)**** *as needed* ***and*** *F1 Form*** completed, signed, and dated by RA or MD*

Follow-up information after 12 and 24 months post the study MRI will only be obtained in the subset of participants with an abnormal finding identified at the initial 12 and 24 month follow-up evaluation. In this group of patients with abnormal findings identified in the 12 and 24 months post MRI, any information from studies (CBE, imaging, pathology) resulting from the abnormal finding at 12 and 24 months will be collected up to 16 months post the initial study MRI. In addition, abnormal findings identified at the 24-month follow-up evaluation will be collected up to 30 months post the initial study MRI.

*** Clinical reports identified as source documentation must include patient's name, date of imaging or procedure, the clinical information, and the signature of the examiner/reader.*

****The image interpretation data beyond that documented in the radiology report may be recorded on the CRF and is accepted as source documentation if signed by the MD (see Section 9.3).*

10.1

The original section 10.1 has been deleted and replaced by the following: "The following images are required to be submitted to ACRIN Image Archive (see address below): 1) all MR images and 2) original mammogram and sonogram ONLY for cases in which cancer has been identified."

10.1.1

The third and fourth sentences have been deleted: "For film submission, all unique patient identifiers must be removed from the film, and the identity of the participant will be reflected as follows: Institution ID, ACRIN Case #, study #. All media and film will be retained by ACRIN Headquarters unless otherwise requested, and return packaging and postage is provided." They have been replaced by the following: All original mammograms will be digitized and returned by overnight courier within 48 hours. "While it is the preference of ACRIN that all patient identifiers be removed from the films to be submitted, we recognize that MQSA requirements may prevent you from doing so. If films are submitted with patient identifiers, they will be masked during the scanning process in order to maintain future patient anonymity."

12.1

In the first sentence, "60 days" has been changed to "90 days." After the first sentence of this section, the following has been added: "If a unilateral mammogram is performed of the study breast, the study breast must be stated to be negative or benign (BIRADS 1 or 2). Separate assessments of each breast are not required in a bilateral mammogram; therefore, if a bilateral mammogram is performed with no

mention of any abnormality of the study breast, the study breast is negative. (Example of a study-eligible mammogram report without mention of the study breast: bilateral mammogram, Impression: Highly suspicious mass in the right breast; biopsy recommended.)"

12.2.1

In the third black bullet, "last post-contrast scan" has been changed to "second post-contrast scan." The following sentence has been added: "Additional post-contrast scans beyond 8 minutes are acceptable at the site's discretion."

A new white bullet has been added, which reads: "Voxel sizes less than 0.9 mm in the frequency encoding direction, less than 1.8 mm in the phase encoding direction, and less than or equal to 3 mm in the slice direction, providing full coverage of the breast of interest. This might be achieved in one of the following ways:" In the next white bullet, "bilateral: FOV 36 cm" has been changed to "Bilateral in axial or coronal planes: FOV 36 cm or less." In the next bullet, "unilateral: FOV 20 cm" has been changed to "Unilateral in axial or coronal planes or bilateral in sagittal plane: FOV 20 cm or less." After the last bullet, a period has been added.

12.2.2

In the third sentence, "the first five scans" has been changed to "the first study scan." In the next sentence, "the MRI QC Committee (Mitch Schnall, Chair)" has been changed to "the Study QC Committee (R. Edward Hendrick, Chair)."

12.5.1

A sentence has been added to this section: "An English translation of the final diagnosis must be submitted with any pathology report originating in a language other than English."

13.3

In the second sentence of the first paragraph, Dr. Hendrick has been added to the committee.

The second paragraph has been deleted. It was replace by the following: "As Chair of the QC Committee, Dr. Hendrick will coordinate image reviews. Prior to opening, a site must submit an MR-guided patient biopsy case to ACRIN for review and approval by Dr. Hendrick; subsequent to opening, the first enrolled case will also be sent to Dr. Hendrick via ACRIN for review. This will allow deviations from protocol and poor quality studies to be discovered at the earliest possible time. Studies that do not meet quality standards will result in notification of the Chair of the Quality Control Committee and the study PI. The site PI and RA will be notified by either the QC Committee Chair or the study PI and asked to submit plans to rectify any systemic problem. In addition, there will be an overread of mammography, sonography, and MRI (if performed because of a cancer identified during the study)."

14.1

In the first sentence of the first paragraph, "undesired, and unplanned" has been added. In the second sentence, "or physiological observation" has been added to the parenthetical, and "regardless of whether it is" has been changed to "that may or may not be". The following has been added to the end of this section:

> *Any symptom, sign, illness, or experience that develops or worsens in severity during the course of the study, including intercurrent illnesses or injuries, should be regarded as an adverse event. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:*

- *Results in study withdrawal*
- *Is associated with a serious adverse event*
- *Is associated with clinical signs or symptoms*
- *Leads to additional treatment or further diagnostic tests*
- *Is considered by the investigator to be of clinical significance*

14.2 and 14.3

These sections have been extensively revised. They now read as follows:

*Adverse events are classified as serious or non-serious. A **Serious Adverse Event (SAE)** is defined as any untoward medical occurrence/AE that is:*

- *Death.*
- *Life-threatening (refers to any adverse event that places the subject at immediate risk of death from the event as it occurred; life-threatening event does not include an event that, had it occurred in a more severe form, might have caused death, but as it actually occurred did not create an immediate risk of death).*
- *Inpatient hospitalization and/or prolongation of an existing hospitalization (hospitalization refers to an overnight admission). Emergency room visits are not considered serious until one of the above criteria is met. Any elective hospitalization for a pre-existing condition that has not worsened does not constitute and SAE.*
- *Persistent or significant disability or incapacity (substantial disruption in a person's ability to conduct normal daily living activities).*
- *A congenital anomaly or birth defect.*
- *Other medically important event.*

Important medical events are those based upon appropriate medical judgment that may not be immediately life-threatening, but are clearly of major clinical significance. They may jeopardize the subject and may require intervention to prevent one of the other serious outcomes noted above.

A pre-existing condition is one that is present at the start of the study. A pre-existing medical condition is defined as an adverse event if the frequency, intensity, or character of the medical condition worsens during the study period. At the screening visit, any clinically significant findings/abnormalities should be recorded as a pre-existing condition. At the end of the study, any new clinically significant findings/abnormalities that meet the definition of an adverse event must also be recorded and documented as an adverse event.

All adverse events that do not meet any of the criteria for serious should be regarded as non-serious adverse events. If there is any doubt whether the adverse event constitutes an SAE, it should be treated as serious.

14.3 Adverse Event Grading

Grade refers to the severity (intensity) of the adverse event:
***1—Mild**: AE is noticeable to the participant but does not interfere with routine activity.*
***2—Moderate**: AE interferes with routine activity but responds to symptomatic therapy/rest.*

***3—Severe**: AE significantly limits the subject's ability to perform routine activities despite symptomatic therapy.*
***4—Life-threatening or disabling**.*
***5—Fatal**.*

14.8.1
The Biomedical Imaging Program (BIP) has been changed to the Cancer Imaging Program (CIP).

14.8.2
"24 hours of the event" has been changed to "24 hours of knowledge of the event."

14.9.1
NCI-BIP has been changed to NCI-CIP.

14.9.2
The name of the program director has been deleted. In the address, Biomedical Imaging Program has been changed to Cancer Imaging Program. In the final sentence, the word "available" has been added.

14.9.4
At the end of the last sentence, "and/or continuing review" has been added. A new sentence has also been added: "Please refer to your local institution's policies regarding AEs, SAEs, and safety reports."

15.0
In the second sentence, "60 days" has been changed to "90 days."

15.4.1
In the table, the third cell in the first row has been changed from "0.55" to "0.055".

Appendix I
Under the heading "Additional Information," the last sentence ("You will be asked for permission to borrow the slides of any biopsies of the study breast obtained since your initial study MRI") has been deleted.

Appendix II
In question #4, "60 days" has been changed to "90 days."

In question #7, the bracketed comments used to read, "[MRI must be within 60 days of CBE, biopsy of initial diagnosis, and mammogram." They now read, "[MRI must be within 90 days of CBE and mammogram, and within 60 days of biopsy of initial diagnosis.]"

In question #14, "or radiation therapy" has been deleted.

In the registration questions, the numbering for #9 and #10 has been switched. In #17, the registration requirement has been changed from one business day to two.

Appendix IV
The draft BI-RADS MRI lexicon has been replaced with an updated version:

APPENDIX IV: ACR–BI-RADS®–MRI Lexicon Classification Form

For each of the following categories, select the term that best describes the dominant lesion feature. Wherever possible, definitions and descriptions used in BI-RADS® for mammography will be applied to MRI of the breast. This form is for data collection and does not constitutes a written MRI report.

LESION TYPE (select one)

A. ***Focus/Foci (Tiny spot of enhancement, < 5 mm) if only finding, GO TO SECTION E***

B. ***Mass (Three-dimensional space-occupying lesion that is one process, usually round, oval, or irregular in shape).***

Shape *(select one)*	***Description***
❑ *Round*	*Spherical or ball-shaped*
❑ *Oval*	*Elliptical egg-shaped*
❑ *Lobular*	*Undulating contour*
❑ *Irregular*	*Uneven shape (not round, oval, or lobulated)*

Margin *(select one)*	***Description***
❑ *Smooth*	*Well-circumscribed and well-defined margin*
❑ *Irregular*	*Uneven margin can be round or jagged (not smooth or spiculated)*
❑ *Spiculated*	*Characterized by radiating lines*

Mass Enhancement *(select one)*	***Description***
❑ *Homogeneous*	*Confluent uniform enhancement*
❑ *Heterogeneous*	*Nonspecific mixed enhancement*
❑ *Rim enhancement*	*Enhancement more pronounced the periphery of mass*
❑ *Dark internal septation*	*Dark nonenhancing lines within a mass*
❑ *Enhancing internal septation*	*Enhancing lines within a mass*
❑ *Central enhancement*	*Enhancement more pronounced at center of mass*

C. ***Non-Mass-Like Enhancement (that is in an area that is not a mass)***

Non-Mass-Like Enhancement *(select one)*	***Description***
❑ *Focal area*	*Enhancement in a confined area, less than 25% of quadrant*
❑ *Linear*	*Enhancement in a line that may not conform to a duct*
❑ *Ductal*	*Enhancement in a line that may have branching, conforming to a duct*
❑ *Segmental*	*Triangular region of enhancement, apex pointing to nipple, suggesting a duct or its branches*
❑ *Regional*	*Enhancement in a large volume of tissue not conforming to a ductal distribution, geographic*
❑ *Multiple regions*	*Enhancement in at least two large volumes of tissue not conforming to a ductal distribution, multiple geographic areas, patchy areas of enhancement*
❑ *Diffuse*	*Enhancement distributed uniformly throughout the breast*

Non-Mass-Like Enhancement (internal enhancement) *(select one)*	***Description***
❑ *Homogeneous*	*Confluent uniform enhancement*
❑ *Heterogeneous*	*Nonuniform enhancement in a random pattern*
❑ *Stippled, punctate*	*Punctuate, similar appearing enhancing foci, sand-like or dot like*
❑ *Clumped*	*Cobblestone-like enhancement, with occasional confluent areas*
❑ *Reticular, dendritic*	*Enhancement with finger like projections extending toward nipple, especially seen on axial or sagittal images, in women with partly fatty–involuted breasts*

D. ***Symmetric or Asymmetric (Bilateral scans only)***

Symmetric or Asymmetric *(select one)*	***Description***
❑ *Symmetric*	*Mirror-image enhancement*
❑ *Asymmetric*	*More in one breast than in the other*

E. Other Findings *(select all that apply)*

Other Findings ***(select all that apply)***

❑	***None apply***	❑	***Edema***
❑	***Nipple retraction***	❑	***Lymphadenopathy***
❑	***Nipple invasion***	❑	***Pectoralis muscle invasion***
❑	***Pre-contrast high ductal signal***	❑	***Chest wall invasion***
❑	***Skin thickening (focal)***	❑	***Hematoma/blood***
❑	***Skin thickening (diffuse)***	❑	***Abnormal signal void***
❑	***Skin invasion***	❑	***Cysts***

F. Kinetic Curve Assessment

Kinetic Curve Assessment	***Description***
❑ *Initial rise*	*Slow, medium, rapid*
❑ *Delayed phase*	*Persistent, plateau, washout*

G. Assessment Category *(select one)*

Assessment Category *(select one)*	***Description***
❑ ***Category 0*** *– Incomplete: Need additional imaging evaluation*	*Finding for which additional evaluation is needed*
Final Assessment	
❑ ***Category 1*** *– Negative*	*No abnormal enhancement, no lesion found (routine follow-up)*
❑ ***Category 2*** *–Benign finding*	*Benign, no malignant features; i.e. cyst, (routine follow-up)*
❑ ***Category 3*** *– Probably benign finding*	*Probably benign finding (short interval follow-up)*
❑ ***Category 4*** *– Suspicious abnormality*	*Low to moderate suspicion for malignancy (biopsy should be considered)*
❑ ***Category 5*** *– Highly suggestive of malignancy*	*High probability of malignancy (appropriate action should be taken)*
❑ ***Category 6*** *– Known cancer*	*Known, biopsy proven malignancy diagnosis on the imaged finding prior to definitive therapy (appropriate action should be taken)*

Appendix V

The Protocol-Specific Application has been expanded and updated. It now reads as follows:

APPENDIX V, revised May 6, 2003

ACRIN PROTOCOL-SPECIFIC APPLICATION

ACRIN 6667 – MRI EVALUATION OF THE CONTRALATERAL BREAST IN WOMEN WITH A RECENT DIAGNOSIS OF BREAST CANCER

*This application is in addition to the ACRIN General Qualifying Application that can be found on the ACRIN web page (**www.acrin.org)**.*

Name of Institution _____
ACRIN P.I. Name _____
Address _____
Address _____
Telephone _____
Fax _____
E-mail _____
Research Associate's Name _____
Name(s) of Radiologist(s) interpreting study mammograms at your site _____
Name(s) of Radiologist(s) interpreting study ultrasounds at your site _____
*Name(s) of Radiologist(s) interpreting study breast MRIs at your site*_____
*Number of breast MRIs interpreted by above radiologist(s) (in order listed above)**

_____ _____ _____

*Name(s) of Radiologist(s) performing breast MR wire locs or biopsies at your site*_____
*Number of breast MR wire locs or biopsies performed by named radiologist(s) (in order listed)***

_____ _____ _____

Have you submitted clinical breast MR image data for a previous IBMC/ACRIN study? Yes ____ No ____

(If no, a clinical breast MR case must be submitted for review for participation in 6667.)

Have you submitted MRI biopsy qualifying data for a previous IBMC/ACRIN study? Yes ____ No ____

(If no, an MRI-guided biopsy patient case must be submitted for review for participation in 6667.)

Do you have Internet access? Yes No

* *Minimum number of 50 per radiologist required for study participation.*
** *Minimum of 5 per radiologist required for study participation.*

*Institution*_____ *Date* _____

MRI Scanner Used for Breast MRI:

Manufacturer _____ *Model* _____ *Field Strength* _____ *Tesla* *Dedicated* *Breast* *Coil?* ☐*Unilateral* ☐*Bilateral*

MR Pulse Sequence Used for Contrast-enhanced Imaging:

Acquisition Plane (Axial, Sagittal, or Coronal)	*Sequence Name* ---------- *2D or 3D? (please check one)*	*Slice Thick-ness (mm)*	*Unilateral or Bilateral (please check)*	*FOV*	*Matrix*	*Chemically-selective Fat Suppression Used?* ---------- *Subtraction Performed?*	*Basic Sequence Duration (i.e., time between end of contrast injection and end of initial post-contrast sequence)*	*Time between end of contrast injection and end of second post-contrast scan*	*TR (ms)*	*TE (ms)*	*Flip Angle (deg)*
	---------- ☐*2D* ☐*3D*		☐*Uni* ☐*Bilat*			☐*Yes* ☐*No* _---------- ☐*Yes* ☐*No*					

Contrast Agent Used: _____ *Dose:*_____ *Rate of Admin:*_____ *Saline Flush?* ☐ *Yes* ☐ *No.* *If yes, volume of saline used:* _____

There are many acceptable methods of performing breast MRI. While multiple methods of MR acquisition will be accepted in this study, the following minimum standard criteria must be met for participation:

- *1.5T or greater magnet and dedicated breast surface coil*
- *Minimum of one pre-contrast and two post-contrast enhanced 3D T1 weighted gradient echo sequences (TR<60 msec; TE<20 msec)*
- *Initial post-contrast images of the study breast must be obtained within 4 minutes of contrast injection with the second post-contrast scan ending no later than 8 minutes following injection. Additional post-contrast scans beyond 8 minutes are acceptable at the site's discretion.*

Both bilateral and unilateral scans, using a 3 mm slice thickness, will be accepted providing the minimum resolution requirements are met:

- *Voxel sizes less than 0.9 mm in the frequency encoding direction, less than 1.8 mm in the phase encoding direction, and less than or equal to 3 mm in the slice direction, providing full coverage of the breast of interest. This might be achieved in one of the following ways:*
- *Bilateral in axial or coronal planes: FOV 36 cm or less with 256x512 matrix. Only in cases in which the recommended FOV of 36 cm is not sufficient to cover the full area of breast tissue, the FOV may be increased to 40 cm.*
- *Unilateral in axial or coronal planes or bilateral in sagittal plane: FOV 20 cm or less with 128x256 matrix. Only in cases in which the recommended FOV of 20 cm is not sufficient to cover the full area of breast tissue, the FOV may be increased to 22 cm.*

- *Acceptable method of fat suppression, including available software to suppress fat signal and/or subtraction methods.*

Person Completing Form: _____ Telephone No.: _____ E-mail:_____

Please submit application to: *ACRIN Administrator, Attn. 6667 PSA*
ACRIN
1101 Market Street, Suite 1400
Philadelphia, PA 19107
Fax: 215-717-0936
E-Mail: colson@phila.acr.org
Electronic copies are preferred

ACRIN 6667
SUMMARY OF CHANGES

April 21, 2003 Amendment #1

Cover Page
"Current Edition" has been changed to "Version Date" to comply with NCI's new policy. The date on this page and every other has been changed to 4/21/03.

PI List
For #19, the capitalization of the e-mail addresses has changed to TJULIAN@wpahs.org and WPOLLER@wpahs.org.

#22 has been added: Northwestern University, R. Edward Hendrick, ehendrick@radiology.nwu.edu.

Eligibility
Third bullet: After "MRI," the following has been added: "and there must be no new breast symptoms for which further evaluation is recommended".

Fifth bullet: "60 days" has been changed to "6 months"; "history of adjuvant chemotherapy for therapeutic measures" has been changed to "history of chemotherapy for cancer".

Final bullet: The words "in either breast" have been added after "FNA".

1.0
The following sentence has been deleted from the first paragraph of the abstract: "For a subset of women, a CBE and mammogram of the study breast will be obtained as part of the study to ensure that results from the mammogram and CBE for all participants are documented within 60 days of the MRI."

2.0
In the fourth paragraph of this section, the third and fourth sentences have been updated. They now read, "In a separate study (Lee, Orel, Woo, et al, Radiology, 2003) the cancer yield of MRI in women with a recent cancer diagnosis and negative contralateral mammogram was found to be 3.8%. In a report by Kuhl et al, MRI revealed suspicious or equivocal lesions in the asymptomatic, contralateral breast in 91 out of 710 patients scanned."

5.2.5
At the beginning, "Patients with" has been added.

5.2.8
After FNA, the words "in either breast" have been added.

5.2.9
This exclusion criterion has been added: "Patients with new breast symptoms within the past 60 days for which further evaluation is recommended."

6.1
The third sentence now reads, "The GQA and the PSA should be faxed or mailed to ACRIN administration at the address found on the PSA; the federal-wide assurance should be faxed to the ACR Regulatory Department at 215-574-0300." A new sentence has been added to the end of the paragraph: "The MR images should be sent to Dr. Connie Lehman at the University of Washington."

8.6.4
The IA form is now the "*Initial* Mammogram Assessment Form."

The IM form has been added to the table:

Post MRI Mammogram Assessment Form **(IM)**	Clinical Site	ACR	*as needed*, site will be notified of addition to case calendar

The H1 form has been added to the table:

Ultrasound Images **(H1)** *as needed*	Clinical Site	ACR	*as needed*, site will be notified of addition to case calendar

The word "Initial" has been added to the title of the M3 form.

The M4 form and B2 forms have been added:

MRI Short Interval Imaging Form (M4)	Clinical Site	ACR	*as needed*, site will be notified of addition to case calendar
MRI Finding Tracking Diagram[c] (B2)	Clinical Site	ACR	*within 8 weeks of registration*

The timing of the ME form has been clarified: "and as otherwise specified for short interval imaging."

The XC and PR forms have been added:

Re-Reader Mammogram Form (XC)	QC Committee Reader	ACR	*as needed*, site will be notified of addition to case calendar
Protocol Variation Form (PR)	Clinical Site/DMC	ACR	*as needed*, site will be notified of addition to case calendar

9.5

The following sentence has been added at the beginning of the section: "These records will be audited only if deemed necessary by the Principal Investigator or by the Quality Assurance reviewer."

9.7

In the table, the M3 and IA forms have had "Initial" added to their names. The Ultrasound form has been changed from IB to IS. The following new rows have been added:

Post-MRI Mammogram Assessment Form **(IM)**		Mammogram Report **(I2) and** signed IA form or signed worksheet (MD signature required)
MRI Short Interval Imaging Form **(M4)**		MRI Report **(ME) and** signed M3 form or signed worksheet (MD signature required)

and

Protocol Variation Form **(PR)**	Reviewed for cases in which a variation has been found.	Completed, signed, and dated by Research Associate.

10.0

The original Section 10 (Image Collection) as been deleted and replaced by this updated version:

10.0 IMAGE COLLECTION

10.1 Wherever possible, all images for this protocol are requested to be provided in digital format. ACRIN has developed software that allows for electronic transmission to the DMC image archive of images that have been scrubbed of all patient identifiers. Individual PC computers with this software installed will be supplied to each participating site. ACRIN will be contacting each site individually to determine their readiness and ability to work with this system. If you have preliminary questions, you may contact either Rex Welsh or Fraser Wilton (215-574-3215) for information about this system. Once readiness has been determined, imaging personnel from ACRIN will coordinate the shipment and installation of the PC computers and train all operating staff on use of the system.

10.1.1 When digitizing and direct transfer or electronic media (CD, disk, tape) of any required film images are not available, original films must be submitted via mail for digitization at the DMC and subsequent entry to the image archive. For film submission all unique patient identifiers must be removed from the film, and the identity of the participant will be reflected as follows: Institution ID, ACRIN Case #, study #. All media and film will be retained by ACRIN Headquarters unless otherwise requested, and return packaging and postage is provided. Mailed film images or images on CD should be addressed and sent as follows:

ACRIN Image Archive
ACRIN 6667 Images
American College of Radiology
1101 Market Street, Suite 1400
Philadelphia, PA 19107
Attn: Anita Murray

10.1.2 Where required, images stored in the ACRIN Headquarters image archive may then be routed to other sites involved, using either FTP or CDROM where appropriate, for purposes of secondary review.

12.4.1

In the last sentence of this section, the word “definitive” has been changed to “concordant.”

12.5.4

In the eighth sentence of this section, “and the slice number that contains the lesions” has been deleted, and “and” has been inserted in between “quadrant” and “distance.”

14.9.2

“EST” has been changed to “Eastern Time.”

14.9.3

“EST” has been changed to “Eastern Time.”

15.4.1
In the first sentence, "in 21 institutions" has been deleted.

References
The original Reference #27 has been deleted and replaced by the following: Lee SG, Orel SG, Woo IJ, et al. MRI Imaging Screening of the Contralateral Breast in Patients with Newly Diagnosed Breast Cancer: Preliminary Results. Radiology 2003; 226:773-778.

Appendix I (Consent)
Under the heading "Investigator's Statement," references to "pathology slides," as well as the final sentence, have been deleted. Those words refer an earlier design of the study and were included in error. We have made several such changes to the consent.

The following sentences have been deleted: "Although routinely used to enhance images of many areas of the body, gadolinium is under investigation for use in breast cancer. The FDA has given permission to study gadolinium for use in breast cancer but has not approved this agent for use in detecting breast cancer." These sentences were deleted because they caused undue confusion as to the status of gadolinium in MRI scanning for breast cancer. In an e-mail dated 7/11/2002, Dr. Robert K. Leedham (Associate Director for Regulatory Health Policy and Programs at the FDA) stated that the FDA would not require a sponsor-investigator IND for study IBMC 6884, the pilot study upon which this study was based. Gadolinium will be used for the same purposes in the present study.

Under "How Long Will I Be in the Study?", in the first sentence "a evaluation" has been changed to "an evaluation."

Under "Reproductive Risks," the statement has been changed from "You should not be or become pregnant while on this study" to "You must not be pregnant when you join this study. Talk with your physician about the risks associated with pregnancy during your cancer treatment."

Under the heading "Confidentiality," in the first paragraph "and" has been inserted before "the Statistical Center." The following has been deleted: "the Pathology Core at the University of Washington Medical Center, Seattle, WA". We have also deleted reference to the FDA in the first and second paragraphs because we have taken out the statement that gadolinium is an investigational drug.

In the first sentence of the third paragraph, "will" has been changed to "may." A period has been added after the word "study," followed by "If so,".

The last paragraph of the "Confidentiality" section has been deleted.

Appendix II
Question #2 has been changed and is now, "Will the study MRI be performed within 60 days of the initial biopsy proven (including FNA) cancer diagnosis?

In study registration question #9, "(not Latino)" has been deleted. The code table numbering has been replaced by check boxes, and the words "(check all that apply)" have been added. The check box for "more than one race" has been deleted.

In question #14, "60 days" has been changed to "6 months."

In question #16, "(date of registration)" has been added.

At the end of the form, "Date" has been changed to "Date form completed," and a line has been added for "Signature of person entering data onto the Web."

Appendix V

In the chart on the second page, the final row has been deleted. The typo "rast" has been changed to "contrast."