August 4, 2011

Amendment 1 reflects the ongoing conduct of the trial and revisions requested by the ACR IRB during their initial review of the protocol.

NOTE: The ACR IRB requested initially that the minimum age requirement for the trial be raised from 25 years to 30 years. The trial team considered this request and at this time has opted to leave the original eligibility requirement as presented because one 25-year-old woman has joined the trial. The trial scientific leadership continues to believe that tomosynthesis may be found to be an improvement over mammography in high-risk women of younger ages with denser breasts.

Cover Page
Amendment 1 and version date August 4, 2011, have been added.

Table of Contents
Page numbers were adjusted to match the current version.

Eligibility, Page 4
A typo in "tomosynthesis" has been corrected.

Sample Size, Page 4
The total number of women to be recruited to the trial has been added at the request of the ACR IRB.

A description of the type of Hologic units used in the trial (Hologic Selenia® Dimensions®) has been added at the request of the ACR IRB.

Section 3.2.2.1, Secondary Aims, Page 9
The secondary aim analysis will compare positive predictive value by lesion instead of sensitivity and specificity.

Section 4.3, ACRIN PA Trials and Hologic, Page 11
A description of the type of Hologic units used in the trial (Hologic Selenia® Dimensions®) has been added at the request of the ACR IRB.

A clause has been added at the request of the ACR IRB identifying Hologic tomosynthesis units as being FDA approved.

Section 5.2.8, Exclusion Criteria, Page 12
The Group B population for the study will have had a screening mammogram prior to enrollment in the ACRIN PA 4006 trial. A parenthetical allowing for this requirement has been added as follows—“(excluding the screening mammography required for Group B)”.

Section 8.1.2, PRIOR TO IMAGING: Eligibility and Registration, Page 17
2nd bullet: “per institutional standard of care” has been moved to ensure site understanding that the pregnancy test can be urine or serum, according to institutional practices, and should be conducted on all women of childbearing potential who join the trial.
Section 8.2.2, Local Reader Clinical Assessment, Page 18
New-4th bullet: Has been added to specify lesions to be collected for the trial, as follows—“Only actionable lesions will be collected for the trial. Lesions not prompting call-back will be excluded.”

Section 8.3.3, Local Reader Clinical Assessment: Sequential Reads, Page 19
New-3rd bullet: Has been added to specify lesions to be collected for the trial, as follows—“Only actionable lesions will be collected for the trial. Lesions not prompting call-back will be excluded.”

Section 8.4.2, Follow-Up Procedures, Page 20
4th bullet: Has been revised to include the name and location online at ACRIN.ORG of the “One-Year Follow-Up Guidelines” document.

Section 8.5, Study Procedures Table, Page 21
1st row, column headers for Group A (Screening) and Group B (Diagnostic): “§” has been added in front of each of the 30-day timeline descriptions.

6th row, 1st column: The description of the study-required pregnancy test has been revised to specify that the test should be conducted per institutional standard of care for women of childbearing potential.

12th row, 1st column: “(actionable lesions only)” has been added to specify which reader results will be submitted to ACRIN.

Section 10.9.2, How to Report, Page 28
Reference to Lia Worley as ACRIN AE Coordinator has been deleted.

Section 15.2.2.2, Secondary Aims, Page 31
Section 15.2.2.2.1: The secondary aim analysis will compare positive predictive value by lesion instead of sensitivity and specificity.

Section 15.2.2.2.2: The analysis for lesion-type characterization has been revised, as follows—“PPV comparisons will be made using marginal regression modeling.” References 13 and 14 were deleted with this revision.

References, Page 34
New-reference #12 has been added; former-references #12 through #14 have been deleted.

Appendix I, Informed Consent Form Template, Pages 36–44
Page 36, under “Why Is This Study Being Done?”:
- New-3rd sentence: Has been added at the request of the ACR IRB to describe the long-term intended impact of the research, as follows—“In the long run, researchers hope to reduce the need for women to return for more procedures to show that cancer is not present.”
- Now-4th sentence: Has been corrected for clarity at the request of the ACR IRB.

Page 37, under “How Many People Will Take Part in the Study?”: At the request of the ACR IRB, the 1st sentence has been revised to describe the total accrual target by Group, as follows—“…; 500 women will join Group A when they are being screened for breast cancer and 50 women will join Group B when they return for diagnosis of abnormal screening findings.”

Page 38, 2nd bullet under “Medical procedures that are being done specifically because you are in this study …”: the typo “a” has been deleted.

Page 39, “Study Schema By Group”: Total accrual target numbers by Group have been added at the request of the ACR IRB.

Page 41, under “Radiation Risks”, 2nd paragraph, 3rd sentence: Has been revised at the request of the ACR IRB, and reads as follows—“The risk of developing cancer from imaging-related radiation is associated with radiation doses much higher than what you will receive for this study.”