

ACRIN Protocol 6661

SUMMARY OF CHANGES

Cover Page

ACRIN Vascular and Interventional Chair, “Gary Dorfman, M.D.”, and his contact information have been deleted.

“Including Amendment #1-7” has been changed to “Including Amendments #1 - 8.”

5.2.1 IRB Approval and Informed Consent, Page 4

ACRIN Headquarters fax number “215-574-0300” has been changed to “215-717-0936”.

6.2.2, Page 5

ACRIN Patient Registration fax number “215-574-0300” has been changed to “215-717-0936”.

8.2 Data Collection Submission, Page 9

The address for data submission has been updated. The change of address for ACRIN headquarters to “1818 Market Street, Suite 1600, Philadelphia, PA. 19103”.

8.3.4 Image Submission, Page 9

The address for image submission has been updated to “1818 Market Street, Suite 1600, Philadelphia, PA. 19103”.

9.1.1, Page 10

In the 2nd sentence, “for ablations in proximity to a neurovascular bundle supplying an extremity or in the spine” has been added and the sentence now reads, “General endotracheal or laryngeal mask anesthesia will not be allowed for ablations in proximity to a neurovascular bundle supplying an extremity or in the spine, since sensorimotor testing must be performed.”

The following statement regarding use of general anesthesia has been added after the 2nd sentence: “However, general anesthesia may be performed at a site where the nerve injury is not of clinical concern, especially if it is requested by the study participant and/or determined it is in the best interest of the participant to use general anesthesia.”

11.0 Tests and Observations, Page 13

In the table, under “Laboratory”, “tumor marker” and its footnote, “c. If baseline tumor markers are out of the normal range, follow at 1 month and 3 months (*e.g. CEA, PSA, CA19-9, CA-125*).” have been deleted.

11.2.2 Laboratory, Page 13

2nd sentence, “Tumor markers if out of normal range at baseline will be measured at one and three months.” has been deleted.

12.0 Adverse Event Reporting, Page 14

In the 2nd paragraph, the following sentence has been revised and now reads, “The revised NCI Common Terminology Criteria Adverse Events (CTCAE) version 3.0 (7/03) must be used to score event severity. The CTCAE version 3.0 and the CTC search tool are available on the CTEP web page (<http://ctep.info.nih.gov>).”

12.2.2, Page 15

“Room 6050” has been added to the address for the submission of the expedited AE reports.

The NCI-CIP 24-hour telephone report contact number and the hours for recorder have been updated and now read, “To make a telephone report, contact NCI-CIP at 301-496-0737, available 24 hours a day (recorder after hours from 4:30 PM to 8:00 AM E.S.T.).”

14.1, Page 21

In the 3rd sentence, “Biomedical Imaging Program (BIP)” has been changed to “Cancer Imaging Program (CIP)”.

14.2, Page 21

In the 1st sentence, “BDMC staff” has been changed to “ACRIN staff”.

14.7 Source Documentation for Audit, Page 23

The table has been extensively revised and now reads:

14.7 Source Documentation for Audit

Form		Data Collection / Time of Submission	Source Documentation
A0	Registration	(SC)- Eligibility checklist must be completed prior to web registration. (A0) At time of registration via the ACRIN web site.	SC - Eligibility checklist completed signed and dated by RA or MD. and/or A0 - Completed, signed and dated by RA, after signed consent.
II	Initial Evaluation Also known as on study form	Due within two weeks of registration	Lab report(s) Pathology report(s) MRI /CT report(s)** Participant History and Physical (H &P) MPACS documented by the MD and/or a medication log Physician progress notes and II - Completed, signed and dated by RA or MD***
TF	RFA Treatment Form	Due post RFA procedure.	RFA procedure report (radiology) and/or Procedure notes (signed and dated by MD/Nurse) and/or TF form - signed and dated by MD***
QP	MPAC Results	This form (QP), completed by the RA, records	The MPACS form(s) completed by the Participant

	Form	<p>the MPAC results that are completed by the Participant. Only the QP gets submitted to ACRIN. The MPACS or pain scales stay at the site.</p> <p>Due: 5 days prior to RFA procedure 14 days post RFA procedure 1 month post RFA procedure 3 months post RFA procedure</p>	<p>are the source document(s) for the QP form(s). and QP form(s) completed, signed and dated by the RA.</p>
FI	Follow-Up Form	<p>There are 3 scheduled follow-up periods.</p> <p>Participant is to complete the DP – Patient Pain Medication Diary Worksheet x3 (daily for one week prior to RFA, and for two weeks after RFA)</p>	<p>Lab report(s) MRI /CT report(s)** Participant History and Physical (H & P) Physician progress notes and/or Treatment notes (including any reported toxicities) DP completed signed and dated by the Participant. (3 pages) and FI - Completed, signed and dated by the RA.</p>

Appendix I Sample Consent for Research Study, Page 27

The “blood test that show tumor marker” has been deleted in the “What Is Involved in the Study?” section.

In the Radiofrequency Ablation Procedure table, “(to include tumor markers if necessary)” has been deleted from the 2nd column for blood tests.

Risks Associated with Radiofrequency Ablation Treatment, Page 28

The following statement “If you and your doctor elect to use sedation (general anesthesia) with the procedure, the risks of using sedation will be reviewed with you in separate consent by the anesthesiologist.” has been added to inform participant if GA is recommended and prescribed.

Appendix IV Participating Institution List, Page 36

This section has been extensively revised and now reads:

Beth Israel -Deaconess Hospital

S. Nahum Goldberg, M.D., Radiology

Brown University

Damian Dupuy, M.D., Radiology

Thomas DePetrillo, M.D., Oncology

Thomas Jefferson University Hospital

Adam Zoga, M.D., Radiology

Wake Forest University Hospital,

Bowman Gray Campus

Ronald Zagoria, M.D., Radiology

William Blackstock, M.D., Radiation Oncology

Leon Lenchik, M.D., Musculoskeletal Radiology

Frank Torti, M.D., Medical Oncology

William Ward, M.D., Orthopedic Surgery

UC Davis

John McGahan, M.D.

Barnes Jewish Hospital

Daniel Brown, M.D.

University of Pennsylvania

S. William Stavropoulous, M.D.

MD Anderson

Kamran Ahrar, M.D.

University of Massachusetts

Sri Shankar, M.D.

University of Miami

Venkataramu Krishnamurthy, M.D.

University of Alabama

Robert Lopez, M.D.

St. Elizabeth's Health Center

Richard Barr, M.D.

Quantum Radiology

Gregory Smith, M.D.

Inova Fairfax Hospital

Alain Drooz, M.D.

Evanston Hospital

Tony Farrell, M.D.

University of South Alabama

Brad Steffler, M.D.

Summary of Changes

ACRIN 6661: Phase II Study of Percutaneous Radiofrequency Ablation of Bone Metastasis Using CT Guidance

#7

April 30, 2003

11.0

The chart has been changed to indicate that history/physical is also required pre-RFA, as well as 1 week, 1 month, and 3 months post-RFA.

Appendix I: Sample Consent

Under the heading “Radiofrequency Ablation Procedure,” in the last sentence before the table, the words “chemotherapy or” have been deleted. A new sentence has been added: “You will be asked not to have chemotherapy for 14 days.”

Appendix II: Protocol-Specific Application

A line has been added for the name of the Research Associate.

Appendix III: Eligibility Checklist

The original question # 22 has been moved to the end of the checklist, and the list has been renumbered accordingly.

Appendix IV: Participating Institution List

Emory has been deleted because it is no longer a participating site.

Summary of Changes

ACRIN 6661: Phase II Study of Percutaneous Radiofrequency Ablation of Bone Metastasis Using CT Guidance

#5

March 5, 2003

3.1.1

In the first sentence, the word “if” has been deleted.

4.2.6

In the first sentence, “chemotherapy” has been deleted. In order to clarify the policy on chemotherapy, we have changed the parenthetical sentence that follows to read, “(Chemotherapy will not be allowed within 14 days prior to and within 14 days post RFA procedure).”

9.1.1

In the second paragraph, in the sentence beginning “If after the first 4min...”, “than” has been changed to “then.”

9.2

The second sentence has been deleted. The third sentence has been reworded to read, “There are three 100 mm-long lines printed for visual analogue self assessment scales measuring intensity of pain (*VASPI*), mood (*VASMOOD*) and pain relief (*VASPR*).” In the sixth sentence: “for 1 (no pain)” has been changed to “from 1 (no pain)”. The seventh sentence has been deleted. In the following sentence, “in person” has been changed to “by the patient.”

11.0

The History/Physical column of the table has been changed to reflect the fact that physicals are required only at baseline.

11.2.1

The first sentence formerly read, “History, performance status, and MPAC will be obtained daily for 14 days, at one month, and three months.” It now reads, “MPAC will be obtained daily for 14 days post RFA, at one month, and three months. History and performance status will be obtained at 1 week, one month, and three months.”

12.1.3

The end of this sentence, “with the attribution (possibly, probably, definitely related) to the protocol treatment” has been deleted and replaced by “regardless of attribution and whether the event was expected or unexpected.”

14.7

In the chart, the submission time for the QP form has been changed from “14 days prior to RFA procedure” to “14 days post RFA procedure.”

Appendix I: Sample Consent

Under the heading “Radiofrequency Ablation Procedure,” in the last sentence of the second paragraph, “with chemotherapy or radioisotopes” has been inserted.

Appendix III: Eligibility Checklist

The checklist has been replaced with the updated checklist that follows:

APPENDIX III

ACRIN 6661

ELIGIBILITY CHECK (page 1 of 3)

Case # _____

(to be provided upon activation)

The following questions will be asked at Study Registration:

- _____ 1. *Institutional person registering case (initials only)*
- _____ (Y) 2. *Have all of the questions on the Eligibility Checklist been completed?*
- _____ (Y) 3. *Is the patient eligible for this study?*
- _____ (Y) 4. *Date the study-specific Consent Form was signed? (Must be prior to study entry)*
- _____ 5. *Patient’s Initials (Last, First)*
- _____ 6. *Verifying Physician (Site PI)*
- _____ 7. *Participant’s ID number (Do NOT utilize a medical record number or radiology-assigned number)*
- _____ 8. *Date of Birth (mm-dd-yyyy)*
- _____ 9. *Ethnic category*
 - 1 *Hispanic or Latino*
 - 2 *Not Hispanic or Latino*
 - 9 *Unknown*
- _____ 10. *Race*
 - 1 *American Indian or Alaskan Native*
 - 2 *Asian*
 - 3 *Black or African American (not Latino)*
 - 4 *Native Hawaiian or other Pacific Islander*
 - 5 *White*
 - 6 *More than one race*
 - 9 *Unknown*
- _____ 11. *Gender*
 - 1 *Male*

2 Female

_____ 12. Patient's Country of Residence

- 1 United States
- 2 Canada
- 3 Other
- 4 Unknown

ELIGIBILITY CHECK (page 2 of 3)

_____ 13. Zip Code (US residents)

_____ 14. Patient's Insurance Status

- 1 Private insurance
- 2 Medicare
- 3 Medicare and private insurance
- 4 Medicaid
- 5 Medicaid and Medicare
- 6 Military or Veterans Administration
- 7 Self-pay
- 8 No means of payment
- 9 Unknown/decline to answer

_____ 15. Will any component of the patient's care be given at a military or VA facility?

_____ 16. Calendar Base Date (mm-dd-yyyy)

_____ 17. Other country of residence, specify:

_____ 18. Treatment Start Date

_____ 19. Registration Date

_____ 20. Name of Medical Oncologist

_____ (Y) 21. Bony metastases with a maximum size of < 8cm

_____ (Y) 22. If spinal metastasis, is the vertebral body cortex between the mass and spinal cord/nerve roots intact?

_____ (Y). 23. Documented metastatic bone disease from primary other than musculoskeletal malignancy, lymphoma or leukemia.

_____ (6-10) 24. Persistent intractable pain as measured by the VASPI pain score on a 0-10 scale.

_____ (Y) 25. Pain originates from a solitary site of bony metastatic disease.

_____ (Y) 26. Radiofrequency treatment will be performed within 5 days of baseline evaluations.

_____ (Y) 27. Platelets are $\geq 70,000/\text{ul}$.

ELIGIBILITY CHECK (page 3 of 3)

_____ (N) 28. Previous or scheduled treatment of metastases with chemotherapy, external beam radiation, or radioisotopes within 30 days immediately prior to RFA treatment. (Chemotherapy will not be allowed until 14 days post procedure.)

_____ (N) 29. Treatment site involves weight bearing long bone of the lower extremity.

_____ (N) 30. Patient has a pacemaker.

_____ (N) 31. Impending fracture or metallic fixation at RFA site.

_____ (Y) 32. Baseline laboratory assessments as described in Section 11.0 performed within 14 days of the RFA.

_____ (Y) 33. Discontinuation of medications in compliance with Section 4.2.3.

_____ (N) 34. Is the treatment site located in the cervical, thoracic or lumbar spine?

Signature of person responsible for data: _____

Signature of person entering data onto the web: _____

Date form completed (mm-dd-yyyy): _____

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CT Guidance
Summary of Changes

#3

April 3, 2002

Risk of including the ablation of vertebral metastases has been addressed in the ICF under “Risks Associated With Radiofrequency Ablation Treatment” with the inclusion of: *“ There is the risk, that if the RF electrode is positioned within the spinal column to treat a tumor, heat from the procedure may cause nerve damage (causing numbness and/or weakness). Again however, image guidance will be used to ensure that the electrode is placed appropriately, avoiding the risk of nerve injury”*.

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Phase II Study of Percutaneous Radiofrequency Ablation of Bone Metastasis Using
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Summary of Changes

#2

March 13, 2002

Eligibility Criteria:

- I. “*Spinal metastases*” has been removed.
- IV. The maximum size of bone metastasis has been changed to 8 cm.
- X. “*Spinal metastasis*” has been removed.

Section 2.0:

Fifth paragraph: “*Spinal RFA for metastatic disease can be safely performed in the presence of an intact vertebral body cortex because cortical bone acts as an insulator and cerebrospinal fluid pulsations as well as the basivertebral venous plexus act as heat sinks to the RF energy*” has been added.

Section 4.1.4:

Maximum size of bone metastasis has been changed from 5 to 8 cm.

Section 4.2.8:

Spinal metastasis has been amended to include “*Spinal metastases that do not have an intact cortex between the mass and the spinal canal and exiting nerve roots*”.

Section 9.1.1:

“*Or reasonable alternatives based on institutional preference*” has been added as part of sedation options.

Second Sentence: “*or in the spine*” has been added.

Second paragraph: “*In patients with spinal metastases the vertebral body cortex between the mass and the spinal canal and exiting nerve root must be intact. An intact cortex will help prevent thermal toxicity to the spinal cord and nerve roots. The site principal investigators will be responsible for determining eligibility based upon the initial CT or MRI examination.*” has been added.

Fourth paragraph: “*5 cm or smaller not involving the spine or weight bearing bones of the lower extremity will enable any radiologist who has performed image guided RFA to successfully achieve the ablation strategy set forth in the methodology*” has been deleted.

Fourth paragraph: “8cm or smaller, and treating spinal metastases that have an intact vertebral body cortex will allow the study to accrue patients who would typically present with poorly controlled pain. Excluding all spinal metastases and treating only smaller tumors would prevent adequate patient accrual because it is unusual for cancer patients to have poorly controlled pain relief with small tumors and many cancer patients have spinal metastases given this common site of spread given the presence of the hematopoietic marrow. Weight bearing bones of the lower extremity will not be treated due to the risk of pathological fracture.” has been added.

Section 13.1:

Last sentence: “Or may benefit from RFA instead of radiation therapy due to the presence of localized disease” has been added.

Appendix II:

Investigator Credentials: “With at least one with the Radionics device” has been added.

Number of RF Ablations Performed: “List number of procedures for each device” has been added.

Number of Bone RF ablations Performed: “List number of procedures for each device” has been added.

Application Submission: Designee has been changed from Irene Mahon to Robert Tew.

Appendix III:

17. Non-spinal has been removed. Maximum size has been amended from 5 cm to 8cm.
18. If spinal metastasis is the vertebral body cortex between the mass and spinal cord/nerve roots intact? has been added, thus changing the numbering of the list. Content has not been altered.

Appendix IV:

- Thomas Jefferson University Hospital.
John Carrino, M.D. has been added.

-UCLA Medical Center
Steven Raman, M.D, has replaced Leanne Seeger, M.D.

The following sites/participants have been included:

UC Davis
John McGahan, M.D.

Barnes Jewish Hospital
Daniel Brown, M.D.

Emory University
Bill Torres, M.D.

SUMMARY OF CHANGES

ACRIN Study 6661

February 6, 2002

The following changes are in effect:

Eligibility:**Changed from:**

“Aspirin and nonsteroidal anti-inflammatory medications, antiplatelet medications, or warfarin must be discontinued at least 7 days prior to the procedure. Low molecular weight heparin preparations must be discontinued 24 hours prior to the procedure.”

To:

“Aspirin and nonsteroidal anti-inflammatory medications, antiplatelet medications, or warfarin must be discontinued prior to the procedure for a time period that is appropriate given the drug half life and the drugs known antiplatelet activity (e.g., aspirin for 7 days and ibuprofen 24 hours). Low molecular weight heparin preparations must be discontinued 24-hours prior to procedure”.

4.2.3:**Changed from:**

“Aspirin and nonsteroidal anti-inflammatory medications, antiplatelet medications, or warfarin must be discontinued at least 7 days prior to the procedure. Low molecular weight heparin preparations must be discontinued 24 hours prior to the procedure”.

To:

“Aspirin and nonsteroidal anti-inflammatory medications, antiplatelet medications, or warfarin must be discontinued prior to the procedure for a time period that is appropriate given the drug half life and the drugs known antiplatelet activity (e.g. aspirin for 7 days and ibuprofen 24 hours). Low molecular weight heparin preparations must be discontinued 24-hours prior to procedure”.