

NCI Community Oncology Research Program – Kansas City **(NCORP-KC)**

NSABP B-51, A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chest Wall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients with Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy

This is a clinical trial, which is a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask the study doctor for more information.

You are being asked to take part in this study because you have had chemotherapy and then breast surgery to treat your breast cancer. Before you received your chemotherapy, you had some cancer cells in your lymph nodes. During the surgery that you had after finishing your chemotherapy, your doctor removed some lymph nodes from your underarm. No cancer cells were found in any of the removed lymph nodes.

Who is conducting the study?

This study is being conducted by NRG Oncology. This study was originally conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the Radiation Therapy Oncology Group (RTOG). NSABP and RTOG have joined with one other clinical trials group to form NRG Oncology as required by the National Cancer Institute.

Why is this study being done?

For women with breast cancer who **do not** have cancer cells in the lymph nodes removed at surgery, radiation is usually given to the breast only after lumpectomy and not at all after mastectomy. For women with breast cancer who **do** have cancer cells in the lymph nodes removed at surgery, radiation is usually given to the breast and lymph nodes after lumpectomy; and after mastectomy, radiation is usually given to the area where the breast used to be and to the lymph nodes.

- The main purpose of this clinical trial is to study women like you who have cancer cells in the lymph nodes at the time that the breast cancer is diagnosed and have chemotherapy before surgery that clears the cancer cells from the lymph nodes. This study asks 1) if, after lumpectomy, radiation to the breast and lymph nodes will be better than radiation only to the breast at keeping breast cancer from returning, and 2) if, after mastectomy, radiation to the area where the breast used to be and to the lymph nodes is better than no radiation at keeping breast cancer from returning.

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- This study also asks whether giving radiation as described above will help women live longer.
- In order to learn more about certain features of cancer tumors and how they respond to treatment, this study includes special research tests that will be done on samples of the tumor tissue. The submission of tumor tissue from your breast biopsy and again at the time of your breast surgery, if any tumor remains in your breast, is a requirement of this study. You cannot participate in this study if you do not agree to tumor submission. Information about these study requirements will be explained to you in more detail later in this consent form.
- This study will help researchers learn about how the study treatment affects your quality of life. Quality of life is your physical and emotional well-being. If you had a mastectomy and breast reconstruction (plastic surgery to restore the shape and appearance of your breast), the study also will learn about the feelings you have about how your breast looks after radiation therapy. Researchers will compare your feelings to women who had a mastectomy and breast reconstruction but did not receive radiation therapy. The study will also look at the quality of life issues related to arm function, arm and breast edema (swelling), breast appearance, pain, fatigue, and restricted work and social activity.

How many people will take part in the study?

About 1,636 women from different cancer treatment centers will take part in this study.

What will happen if I take part in this research study?

Before you begin the study:

You will need to have the following tests and exams to find out if you can be in the study. These tests and exams are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- History and physical exam
- Breast exam
- Blood tests to check your blood counts
- Pregnancy test if you are a woman of childbearing potential
- Mammogram or MRI of both your breasts or possibly one breast if you had a mastectomy
- CT scan of your chest, abdomen, and pelvis and a bone scan or a PET/CT scan may be done if you have not had one of these scans since you learned that you had breast cancer

During the study:

If all the required tests and exams show that you can be in the study and if you choose to take part, you will be “randomized” to one of the study arms described below. Randomization means that you are put into a study arm by chance.

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A computer program will place you in one of two study arms. Neither you nor your doctor can choose the study arm you will be in. You will have an equal chance of being placed in either study arm.

- If you are in Arm 1 and had a lumpectomy, you will receive radiation to your breast. If you had a mastectomy, you will not receive radiation therapy.
- If you are in Arm 2 and had a lumpectomy, you will receive radiation therapy to your breast and lymph nodes. If you had a mastectomy, you will receive radiation to the area where your breast used to be and to the lymph nodes.

You will begin your radiation therapy within 12 weeks after your surgery or after chemotherapy if you received it after surgery. You should be able to do most or all of your daily activities between treatments. Radiation does not stay in your body between treatments or after the final treatment, but the effects of radiation may continue for several weeks after your final treatment.

If you are randomized to receive radiation therapy, you will receive it according to one of the following schedules.

Arm 1 (Group 1A Lumpectomy):

You will have radiation therapy to your whole breast once a day for five days a week for five weeks. You will *not* receive radiation therapy to your lymph nodes. Then you will have radiation therapy to the area of the lumpectomy alone for an additional 1 to 1½ weeks as determined by your doctor.

Arm 1 (Group 1B Mastectomy):

You will *not* receive radiation therapy. Your doctor will discuss other therapy that you will receive.

Arm 2 (Group 2A Lumpectomy):

You will have radiation therapy to your whole breast and lymph nodes once a day for five days for five weeks. Then you will have radiation therapy to the area of the lumpectomy alone for an additional 1 to 1½ weeks as determined by your doctor.

Arm 2 (Group 2B Mastectomy):

You will have radiation therapy to the area where your breast used to be and to your lymph nodes once a day for five days a week for five weeks.

Other therapy

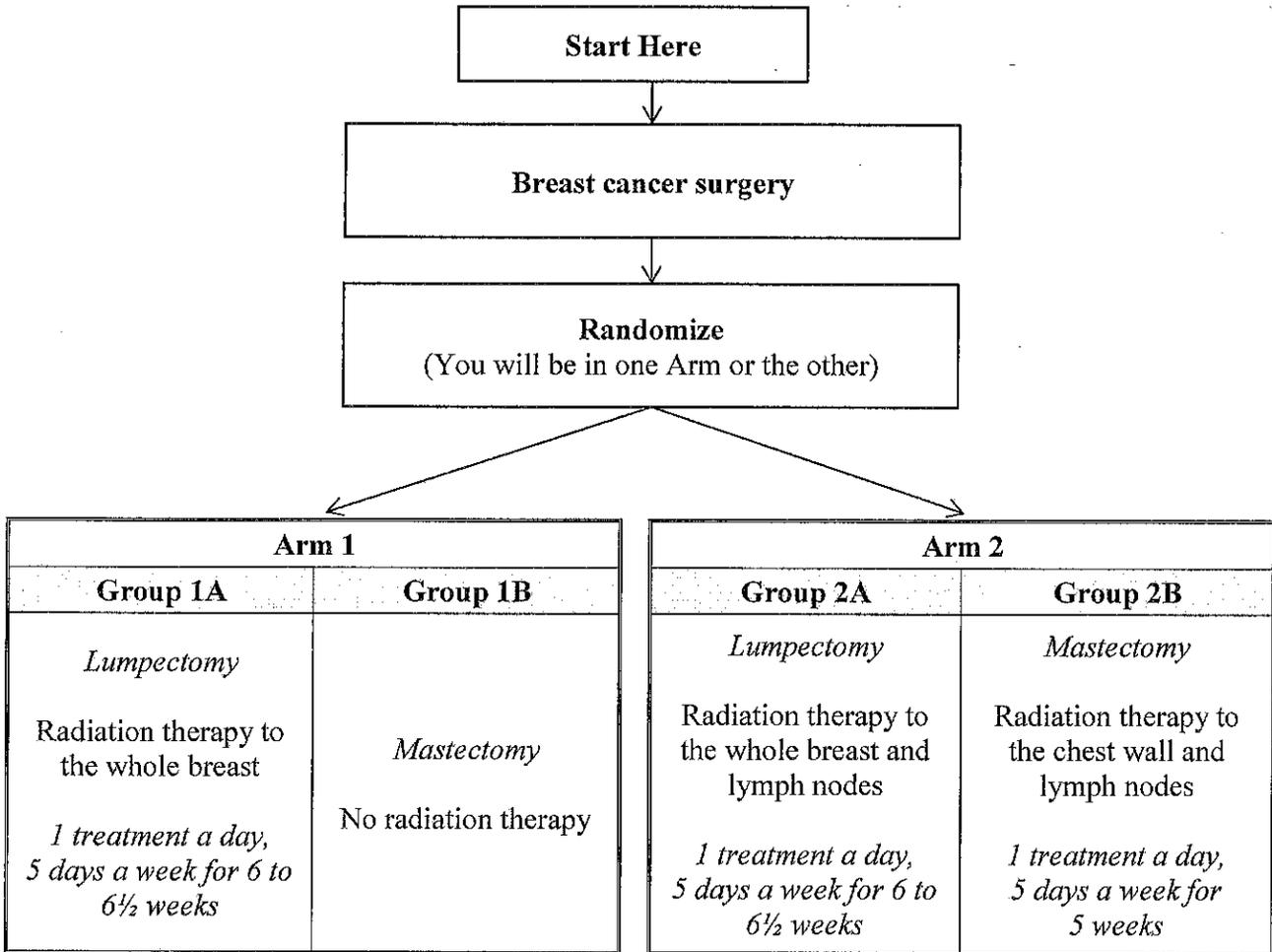
Hormonal therapy: If your breast cancer is affected by hormones (estrogen or progesterone), your doctor will also want to give you at least 5 years of hormonal therapy. Hormonal therapy may be started before, during, or after radiation therapy. Your doctor will discuss this further with you.

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Study Plan

One way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



Anti-HER2 therapy such as trastuzumab: If you received anti-HER2 therapy with the chemotherapy that you received before you had your surgery, your doctor may decide to continue the anti-HER2 therapy after your surgery. Your doctor will discuss this further with you.

Tests and exams during study therapy:

You will need to have the following tests and exams. They are part of regular cancer care.

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- Physical exams on a regular basis during radiation therapy and after your last dose of radiation therapy

Follow-up tests and exams:

You will need to have the following tests and exams. They are part of regular cancer care.

- Physical exam about every 6 months until 2 years after you joined the study and then every 12 months until 10 years after you joined the study.
- Mammogram about every year until 10 years after you joined the study.

Quality of life questionnaires:

You may be asked to complete a questionnaire about any symptoms you are having and about your quality of life (your physical and emotional well-being). We want to learn about your view of how your life is affected by the study treatment and its side effects. This quality of life study will collect information from you about how you are feeling physically and emotionally during your study therapy. We also want to learn how well you are able to carry out your day-to-day activities. In addition, you will be asked questions about how satisfied you are with the appearance of your breast after surgery and radiation therapy, if you received it. The questionnaire will take about 20–30 minutes of your time to complete. You will be asked to complete this questionnaire 5 times: before you join the study, at the end of radiation therapy if you are in Group 1A, 2A, or 2B or at 3 months after you joined the study if you are in Group 1B, and at 6 months, 1 year, and 2 years after you joined the study. If any questions make you feel uncomfortable or you do not wish to answer them, you may skip those questions and not give an answer. You will be asked about whether or not you would like to participate in the QOL questionnaire later in this consent form.

How long will I be in the study?

If you receive radiation therapy, your radiation therapy will take approximately 5 to 6½ weeks depending in which Group you are placed. After you complete your study therapy or if you are in Group 1B, your study doctor will ask you to visit the office for follow-up exams (as described above) for 10 years from the time you joined the study. You should continue yearly mammograms after that for the rest of your life. We would like to keep track of your health for 10 years. Keeping in touch with you and checking on your condition helps us to look at the long-term effects of the study therapy.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. It is important to tell the study doctor if you are thinking about stopping so any risks from the therapy can be evaluated by your doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss the follow-up care and testing that would be best for you.

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You can choose to stop in one of two ways:

- You can stop your study treatment, but still allow your study doctor to report your health status to the NSABP; or
- You can stop your study treatment and request that no new information be reported to the NSABP.

Also, your study doctor may stop you from taking part in this study if he or she believes it is in the best interest of your health, if you do not follow the study rules, or if the study is stopped by the NSABP and RTOG.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Most of these are listed here, but there may be other side effects that we cannot predict. Side effects will vary from person to person.

Everyone taking part in the study will be watched carefully for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop radiation therapy. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects related to radiation therapy:

Likely

These side effects occur in **10% or more** of patients:

- Reddening of the skin during treatment and for several weeks following treatment
- Tanning of the skin lasting months and may be permanent
- Slightly smaller breast size or change in the way the breast looks
- Mild thickening or firming of the breast on touch
- Tiredness and weakness during treatment and for several weeks following treatment
- Swelling of breast
- Peeling of the skin in the area treated with radiation
- Mild pain at the site of radiation treatment requiring over the counter pain relievers

Less likely

These side effects occur in **3–9%** patients:

- Soreness or tightness in muscles of the chest wall under the treated breast
- Severe pain at the site of radiation treatment requiring prescription pain relievers
- Prominent thickening or firming of the breast on touch

Rare but serious

These side effects are **rare but serious**, occurring in **less than 3%** of patients:

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- Cough
- Difficulty breathing
- Inflammation of the heart muscle
- Increased risk for heart disease for patients with cancer in the left breast
- Rib fracture
- Risk of developing another cancer

Reproductive risks: You should not become pregnant while receiving radiation therapy because the radiation therapy in this study can affect an unborn baby. It is important that you understand that you need to use birth control while receiving radiation therapy. Check with your study doctor about what kind of birth control methods to use and how long to use them. If you feel you might be pregnant, even though you practiced birth control, you must notify your study doctor immediately. Ask about counseling and more information about preventing pregnancy.

You should also not breastfeed while receiving radiation therapy.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope that administering radiation therapy to the breast and lymph nodes in patients who had a lumpectomy or giving radiation therapy to the area where the breast used to lie and the lymph nodes in patients who had a mastectomy will be more useful in treating breast cancer compared to radiation to the breast for lumpectomy patients and no radiation in patients who had a mastectomy, there is no proof of this yet. We do know that the information from this study will help doctors learn more about giving radiation therapy to only the breast in lumpectomy patients or no radiation therapy in mastectomy patients. This information could help future breast cancer patients.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting treatment or care for your cancer without being in this study
- Taking part in another study
- Getting no treatment

Talk to your study doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

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Some of the coded research information may be sent to a central database. The information will continue to be made available for approved research. Your name or contact information will not be put in the database.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The study sponsor, NRG Oncology;
 - Alliance for Clinical Trials in Oncology;
 - ECOG-ACRIN Cancer Research Group;
 - a local Institutional Review Board (IRB), a group of people who review the research study to protect your rights
 - the Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to clinical trials; and
 - government agencies, including the NCI or its authorized representatives, the Food and Drug Administration, the Office for Human Research Protections (OHRP), and Health Canada.
- These agencies may review the research to see that it is being done safely and correctly.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What are the costs of taking part in this study?

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

You will not be paid for taking part in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://cancer.gov/clinicaltrials/learningabout/payingfor>. You can print a copy of the information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, _____ [*investigator's name(s)*], if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call him/her at _____ [*telephone number*].

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

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What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

The Data Monitoring Committee (DMC), an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. You may be asked to sign another consent form in response to new information.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ [name(s)] at _____ [telephone number].

For questions about your rights while taking part in this study, call the NCI Community Oncology Research Program-KC Institutional Review Board (a group of people who review the research to protect your rights) at 913-948-5588.

Tumor Collection for the NSABP B-51/RTOG 1304 Study

How will samples of my tumor be used for research?

Required submission of tumor: By signing this consent form, you are agreeing to have a small sample of tumor from the biopsy that showed you had breast cancer and a small sample of any tumor larger than 0.5 cm (about a quarter of an inch) that was found when you had breast surgery sent to the NRG Oncology. These samples will be used for the research purposes of the B-51/1304 study and are required in order to participate in this study. The tumor sample will be stored at the NRG Oncology. Some of the research tests will be done soon, but others will be done in the future when the best methods to test the samples are ready.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people related to you. Researchers are interested in how genes affect health and disease, and how genes affect the return of tumors and how your body responds to treatment.

If you choose to take part in this study, your tumor samples from the B-51/1304 study will be stored at a Biobank being run by the NRG Oncology and supported by the National Cancer Institute. Storing samples is called biobanking.

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What is involved?

If you agree to take part, here is what will happen next:

- 1) A sample of tumor from the biopsy that showed you had breast cancer and a sample from the tumor at the time of your surgery, if collected, are required to be sent to the Biobank for research purposes of the B-51/1304 study. Samples and some related information may be stored in the Biobank, along with that from all the other people who take part. The samples will be kept until they are either used up or destroyed.
- 2) Qualified researchers can submit a request to use the samples stored in the Biobank for B-51/1304 studies. A science committee at the NSABP, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the study is necessary and proper. Researchers will not be given your name or any other information that could identify you.
- 3) Neither you nor your doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
- 4) Some of your genetic and health information may be placed in central databases that may be public, along with similar information from many other people. Information that could directly identify you will not be included.

What are the possible risks?

- 1) There is a risk that someone could get access to the personal information in your health record or other information we have stored about you.
- 2) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. We believe the chance that someone will identify you is very small. But the risk may change in the future if people come up with new ways of tracing information.
- 3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. We believe the chance these things will happen is very small, but we cannot make guarantees.

How will information about me be kept private?

Your privacy is very important to us, and we will make every effort to protect it. Here are just a few of the steps we will take:

- 1) When we send samples to approved researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a code number only.
- 2) We will keep the list that links the code number to your name separate from your sample and information. Any NRG Oncology staff with access to the list must sign an agreement to keep your identity confidential.

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- 3) Researchers to whom the NRG Oncology sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
- 4) We will not give information that identifies you to anyone, unless required by law.
- 5) If research results are published, your name and other personal information will not be given.

What are the possible benefits?

You will not benefit from taking part. We hope the researchers make discoveries that might help people in the future.

Are there any costs or payments?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind?

If you decide you no longer want your samples to be used, you can call your study doctor _____ [name(s)] at _____ [telephone number], who will let the Biobank know. Then, any sample that remains in the bank will no longer be used. Related information that has already been given to or used by researchers cannot be withdrawn. Samples may not be able to be returned or destroyed.

What if I have more questions?

If you have questions about the use of your samples for research, contact your study doctor _____ [name(s)] at _____ [telephone number].

Required use of tumor samples for the NSABP B-51/RTOG 1304 study:

I understand that by signing this consent form, my tumor sample will be used for research related to the B-51/1304 study. I understand that this is required for me to take part in the study.

Optional Quality of Life Study

1. I choose to take part in the Quality of Life Study. I agree to fill out five Quality of Life Questionnaires.

YES

NO

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Permission to contact you in the future

Remember, no matter what you decide, you may still take part in the B-51/1304 study.

2. My doctor or someone from my hospital may contact me in the future to ask me to take part in more research.

YES

NO

Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at <http://cancer.gov/>

- For NCI's clinical trials information, go to: <http://cancer.gov/clinicaltrials/>
- For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>

You will receive a copy of this form. If you want more information about this study, ask your study doctor.

Release

By signing this form you authorize NCORP-KC to access and obtain information that is required for the study. This may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

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My Signature Agreeing to Take Part

I have read this informed consent form or had it read to me. I have discussed it with the research team and my questions have been answered. I will be given a copy of this form. I agree to take part in the B-51/1304 study.

Date

Patient's signature

Print patient's name

Date

Signature of person conducting the
informed consent discussion

Print name of person conducting the
informed consent discussion

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