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CONSENT FORM AND AUTHORIZATION FOR DISCLOSURE OF PROTECTED HEALTH INFORMATION

STUDY TITLE: PHASE I FEASIBILITY STUDY OF LOW DOSE WHOLE BRAIN IRRADIATION IN THE TREATMENT OF ALZHEIMER'S DISEASE

Principal Investigator: **James Fontanesi, MD**
Address: **27900 Grand River Ave.**
Suite 120
Farmington Hills, MI 48336

Hospital: Beaumont, Farmington Hills

INTRODUCTION

Why is this study being done?

You are being asked to participate in a research study. The purpose of clinical research is to look at the nature of disease and try to develop improved methods to diagnose and treat disease. The doctor or clinician in charge of the study believes you meet the initial requirements to take part in the study. Before agreeing to participate, it is important for you to read and understand the following explanation of the research procedures. This Consent and Authorization form describes the purpose, procedures, benefits, risks and discomforts of the study. It also describes the alternatives available to you, and your right to withdraw (quit) from the study at any time.

Please read this information carefully and ask as many questions as you like before deciding whether or not you would like to take part in this research study.

The goal of this study is to evaluate what effects, good and/or bad, that low dose whole brain radiation will have on memory and thinking in participants who have a diagnosis of Alzheimer's Disease. In this study you will get whole brain irradiation (exposure to radiation) and you will receive either 5 or 10 treatments that will be delivered on a daily basis Monday through Friday. Long term radiation effects, those which may occur after one year, will not be assessed in this study. The use of radiation to treat Alzheimer's Disease has not been approved and is considered investigational.

The study doctors expect to enroll 30 participants at 2 institutions in Michigan, with 15 patients at Beaumont, Farmington Hills.

How long will I be in the study?

If you decide to take part in this study, your participation is expected to last from enrollment through the last follow-up visit which will take about 1 year.

DESCRIPTION OF THE STUDY

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

You are being asked to take part in this research study because you meet the criteria for this study and have been diagnosed with probable Alzheimer's Disease.
You will receive whole brain irradiation using standard external beam techniques. This type of radiation delivers treatment to your whole brain from two different directions while blocking radiation to your eyes, nose, throat, and the lower part of your neck. All patients will receive 1 treatment per day on consecutive days excluding weekends. The first 15 patients consented will be assigned to Group 1 and the last 15 patients consented will be assigned to Group 2.

Group 1 (participants 1-15):

If you are in Group 1 you will receive 5 treatments on consecutive days of radiation therapy (Dose Level 1 [5 x 200 cGy]) to the whole brain Monday through Friday.

Group 2 (participants 16-30):

If you are in Group 2 you will receive 10 treatments on consecutive days of radiation therapy (Dose Level 2 [10 x 200 cGy]) to the whole brain Monday through Friday.

Study Procedures

This study will not only involve receiving treatment to the whole brain but will require baseline and follow-up testing to determine if there is progression of the neurocognitive/memory issues that are often seen in patients with Alzheimer's Disease.

Pretreatment

You will need to have the following tests and evaluations prior to the initiation of treatment and after signing this Consent and Authorization form. You may not meet the criteria required by the study. These tests will determine your eligibility to continue participation in the study. These tests and procedures include the following:

- Consultations with dementia specialists to assess your suitability for the study which will occur in the Neuroscience Building at Beaumont, Royal Oak.
- MMSE (Mini Mental Status Exam to check neurocognitive/memory issues) is a 30-point questionnaire and will take approximately 5-10 minutes to complete.
- ADAS-Cog (Alzheimer's Disease Assessment Scale-cognitive subscale to check neurocognitive/memory issues) consists of 11 parts and takes approximately 30 minutes to complete.
- History and Physical Exam
- QOL-AD (Quality of Life-Alzheimer's Disease) is used to assess your quality of life with Alzheimer's and will take approximately 10-15 minutes to complete.
- QUALID (Quality of Life in Late Stage Dementia) is used to assess your quality of life with late stage Alzheimer's disease and other dementing illnesses and will take approximately 5 minutes to complete.

After the above assessments, on a separate day, you will be scheduled and have a pre-treatment Amyvid (Florbetapir-F18 Injection) PET (Positron Emission Tomography) Scan (a 10-minute PET image will be done 30 to 50 minutes after the Amyvid injection) to determine status of Alzheimer's Disease. This will be done in the Adaptive Imaging Suite, a research suite located in the lower level of the Beaumont, Royal Oak main hospital. When you are deemed eligible by the pre-treatment visits, then you will have a consultation with the radiation oncologist which will include baseline assessment, history and physical. The radiation oncologist will set up your study treatment planning at this visit.

Radiation Planning and Treatment

- Radiation planning/simulation: This is a standard part of receiving radiation to the head. During this appointment, you will lay on a flat table attached to a CT scanner (which takes pictures of the inside of your body). A material that is made out of plastic with holes in it (so you can see and breathe) will be placed over your face and neck. This material will follow the shape of your face and allow the radiation oncology department to put your head in the same position on the radiation machine every day. This face mask is a mold of your face, used only by you. The radiation therapy simulation process will last about 1 hour and 30 minutes. You will not receive any radiation (treatment) on this day because it takes several days to plan a safe radiation case.

- Radiation Treatment: Once your radiation treatment plan is ready (usually within a few days but may take up to two weeks), you will begin your treatment. You will lie in the same position that you were in for the measurement session (radiation simulation) that occurred just a few days earlier. You will not feel anything while the radiation is being delivered. Sometimes radiation can cause side effects, but this usually occurs several days later after you have received several doses of radiation. You will be receiving a total of 5 or 10 doses of treatments with radiation therapy. Each treatment takes about 10 minutes. You can expect to be in the radiation oncology department about 30-45 minutes each day (which includes checking in at the front desk, getting changed, getting positioned on the treatment machine and time for you to walk back out to your car).

- Daily, while you are in the clinic for your radiation, you will meet with the radiation doctor to discuss your symptoms and how treatment is going.

- On Day 5 of your radiation treatment, the radiation oncologist will assess for any side effects (toxicities) that are expected or that you may be experiencing.

Post treatment

After treatment is complete you will need to have the following tests and procedures during your 12 month follow up period:

- ADAS-Cog at 6 weeks, 3, 6, and 12 months post treatment (to check neurocognitive/memory issues)
- MMSE at 6 weeks, 3, 6, and 12 months post treatment (to check neurocognitive/memory issues)
- History and Physical Exam at 6 weeks, 3, 6, and 12 months post treatment
- Amyvid PET Scan at 4 months post treatment
- Evaluation for side-effects at 6 weeks, 3, 6, and 12 months post treatment
- QOL-AD (Quality of Life-Alzheimer's Disease) at 6 weeks, 3, 6, and 12 months post treatment
- QUALID (Quality of Life in Late Stage Dementia) at 6 weeks, 3, 6, and 12 months post treatment

Study Calendar

	Pre Treatment	Day 5 of Radiation Therapy	6 Weeks Post Treatment	Post Treatment (Months)			
				3	4	6	12
ADAS-Cog	X		X	X		X	X
MMSE	X		X	X		X	X
History & Physical	X		X	X		X	X
AMYViD PET scan	X				X		
Toxicity Evaluation	X	X	X	X		X	X
QOL-AD and QUALID	X		X	X		X	X

FDA Clinical Trial Information

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.

RISKS, SIDE EFFECTS AND DISCOMFORTS
Ask your physician what the standard of care risks are as well as the study risks.
What side effects or risks can I expect from being in the study?

Risks of Whole Brain Radiation:
Most Frequent (occurring more than 10% of the time):

- Hair loss, which may be permanent
- Dry mouth and/or change in taste
- Headaches
- Nausea and/or vomiting
- Scalp reddening or tanning and irritation
- Memory loss, which can occur in the first few months after whole brain radiotherapy and may be permanent
- Tiredness

Less Frequent (occurring from 1% to 10% of the time):

- Numbness or tingling in feet, legs, arms, or hands
- Loss of deep tendon reflexes
- Skin rash (flat, red area on the skin that is covered with small bumps)
- Drainage of clear fluid from the ears or plugging of the ears with decreased hearing
- Behavioral change and/or increased sleepiness (occurring four to ten weeks after radiation therapy is complete and lasting for several days up to two weeks)
- Cataracts and eye damage with the possibility of impaired vision
- Anxiety or depression
- Constipation
- Agitation

Rare (occurring less than 1% of the time):

- Severe local damage to or death of normal brain tissue, which may require surgery to remove
- Hardening of the arteries in the brain which may lead to strokes
- Eye damage with the possibility of permanent blindness
- Problems with coordination
- Severe confusion
- Developing a new tumor

Risks of Amyvid (florbetapir-F18 injection):
Most Frequent (occurring 2% of the time):

- Headache

Less Frequent (occurring from 1% to 2% of the time):

- Musculoskeletal pain (pain that affects the muscles, ligaments and tendons, and bones)
- Fatigue
- Nausea

Risks of the face mask used for radiation therapy:
Most Frequent (occurring more than 10% of the time):

- Discomfort

Less Frequent (occurring from 1% to 10% of the time):

- Claustrophobia (fear of being in closed or small spaces)

Risks of IV insertion during PET scan (a soft tube will be placed in one of your veins to deliver fluid and/or medication):
Most Frequent (occurring more than 10% of the time):

- Pain and bleeding
- Bruising at needle puncture site

Rare (occurring less than 1% of the time):

- Blood clot
- Infection
- Feeling light headed
- Fainting

There is a rare risk of breach of confidentiality (release of information which personally identifies you).

Not all possible effects are known. With any therapy, unusual, unexpected or previously unreported side effects may occur. You will be informed of any significant new findings, which develop during the course of this research study which may change your decision to continue participating in this study.

Radiation Risk Statement

In addition to the radiation treatment to your brain, this research study involves exposure to radiation from two diagnostic PET scans of the brain. The amount of radiation exposure that you will receive from these scans is 1.6 cGy. A cGy is a unit of radiation dose. This would be at most 0.2% of the treatment dose. Long term radiation effects, those which may occur after one year, from brain radiation are unknown.

BENEFITS

What are the benefits of taking part in this study?

Taking part in this study may or may not make your health better. Doctors hope that the use of low dose whole brain irradiation may eliminate or substantially reduce the accumulation of the specific protein known as amyloid that is thought to cause Alzheimer's Disease. However there is no proof of this in humans. We do know that the information from this study will help the doctors learn more about the effects of whole brain irradiation on patients who suffer from Alzheimer's Disease.

ALTERNATIVE OPTIONS

What are my choices other than taking part in this study?

You do not have to take part in this study to receive treatment for your condition. If you decide not to participate in this study you will receive the usual course of treatment for Alzheimer's Disease performed by your primary care physician.

Your other choices may include:

- Getting treatment or care for your Alzheimer's Disease without being in a study
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative/hospice care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by Alzheimer's Disease. Comfort care tries to keep you as active and comfortable as possible.

ECONOMIC CONSIDERATIONS

What are the costs of taking part in this study?

There is no additional cost to you for participating in this study. The MMSE, ADAS-Cog, Amyvid PET scans, QOL-AD, QUALID testing, history and physical, consultations, and whole brain radiation required for this study will be covered by the study.

COMPENSATION

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

Your involvement in this study is voluntary. The possible risks and side effects which might occur during the course of the research study have been described in this Consent and Authorization form.

A research injury is any physical injury or illness caused by the medications, devices, or procedures required by the study which are administered, used, or performed appropriately. These medications, devices, or procedures are different from the medical treatment you would have received if you had not taken part in the study.

Should you experience a research injury, there are no designated funds provided for subsequent medical care or compensation by either the study doctor/clinician or Beaumont.

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

You are not giving up any of your legal rights by signing this form.

CONFIDENTIALITY, DISCLOSURE AND USE OF YOUR INFORMATION

Will my medical information be kept private?

In order for this research study to take place, you must also authorize the researchers to access and use some of your protected health information (PHI). PHI is information which could identify you as an individual such as name, address, date of birth, etc. By signing this Consent and Authorization Form, you give William Beaumont Hospital permission to use and/or

disclose (release) your health information related to this research. Your medical and billing records collected for the purpose of the study will remain confidential, but may be disclosed (released) or used by the following and/or their representatives:

- The investigators (study doctor/clinician, research staff)
- William Beaumont Hospital
- The Food and Drug Administration
- Other governmental regulatory agencies (domestic and/or foreign)
- Your health insurance company and/or group health plans and their intermediaries (companies contracted to process claims) may also have access to your medical and billing records of the study.

The purpose for this disclosure (release) or use is, for example, to assure compliance with the study protocol, to evaluate the effectiveness of the study, and/or to provide protection to you as a research study participant. The disclosure and use of your information will continue after your involvement in the study has ended. There is no expiration date for the use of your medical and billing records from the study. Any information about you disclosed to the parties identified above may be re-disclosed by them; however, such re-disclosure is not under the protections of this Consent and Authorization.

You will not be identified in any publication or other release of study results, data, and other information (such as in professional writings, at professional meetings, and in the study sponsor's product information, and/or advertising or other promotional materials).

If you decide to withdraw your authorization for the researchers to access and use your personal health information before the end of the study, you will be withdrawn from the research study. However, where the study relied on your Consent and Authorization for the time you participated in the study, your Consent and Authorization cannot be withdrawn and the information already collected may still be used and disclosed as you previously authorized.

STOPPING STUDY PARTICIPATION

What if I decide to stop taking part in the study?

Taking part in this research study is completely voluntary. You may choose not to take part or to stop being in the study (withdraw) at any time without penalty or loss of benefits to which you are otherwise entitled, or without jeopardizing your medical care by your physician at Beaumont. However, if you do not agree to sign this Consent and Authorization form, you will not be able to take part in this study.

If you decide to withdraw from the study you will need to notify the study doctor/clinician of your decision to stop taking part in the study. Written notification is preferred. This notice may be sent to James Fontanesi, MD at Botsford Radiation Oncology Center, 27900 Grand River Avenue, Suite 120, Farmington Hills, MI 48336.

Your participation in this study may be stopped by the study doctor/clinician or study sponsor, without your consent, for any reason, which will be explained to you. Examples include:

- The study medication or procedures appear to be medically harmful to you.
- You fail to follow directions for participating in the study.
- It is discovered you do not meet the study requirements.
- The study is canceled.
- It is determined to be in your best interest (for example, your disease has progressed despite treatment).

CONTACTS

Who can answer my questions about the study?

You may talk to the study doctor/clinicians about any questions or concerns regarding your study participation, or you think you may have suffered a research-related injury. The doctor in charge of the study James Fontanesi, MD may be reached at: 248-471-8120 to answer your questions. Your contact person is Evie Russell, RN. You may contact her at 248-898-5388 or page her at 248-995-1665.

If you have questions regarding your rights as a research participant, or have problems, concerns, complaints, want information or would like to offer input, you may contact the Institutional Review Board Chairperson at (248) 551-0662. The Institutional Review Board is charged with the oversight of all human participant research conducted at William Beaumont Hospital facilities.

STATEMENT OF VOLUNTARY PARTICIPATION

I have read the above, have asked questions and have received answers about this study to my satisfaction. I understand what I have read and willingly give my consent to participate in **PHASE I FEASIBILITY STUDY OF LOW DOSE WHOLE BRAIN IRRADIATION IN THE TREATMENT OF ALZHEIMER'S DISEASE**. I understand I will receive a signed copy of this document and will be promptly informed of any new findings regarding this study. I further authorize the use or disclosure of my health and personal information contained in records as described above.

_____
RESEARCH PARTICIPANT NAME (PLEASE PRINT)

_____ _____ _____
RESEARCH PARTICIPANT SIGNATURE DATE TIME

ALTERNATIVE SIGNATURE (IF RESEARCH PARTICIPANT UNABLE TO SIGN)
AS THE PERSONAL/LEGAL REPRESENTATIVE OF THE STUDY PARTICIPANT, PLEASE PRINT PARTICIPANTS NAME ABOVE IN THE RESEARCH PARTICIPANT SECTION, AND CHECK ONE OF THE BOXES BELOW AS THE BASIS FOR YOUR AUTHORITY TO SIGN THIS CONSENT AND AUTHORIZATION:

☐ COURT-APPOINTED GUARDIAN ☐ DURABLE POWER OF ATTORNEY ☐ NEXT OF KIN
*COURT LETTER IS REQUIRED *ATTORNEY LETTER MUST BE PRESENT & VERIFIED BY 2 PHYSICIANS

_____ _____
NAME (PLEASE PRINT) RELATIONSHIP TO PARTICIPANT

_____ _____ _____
SIGNATURE DATE TIME

*** WITNESS TO THE ENTIRE CONSENT PROCESS AND SIGNATURE ARE REQUIRES IF THE PARTICIPANT IS VISUALLY IMPAIRED, ILLITERATE OR NON-ENGLISH SPEAKING ONLY**

_____
WITNESS NAME (PLEASE PRINT)

_____ _____ _____
WITNESS SIGNATURE DATE TIME

AUTHORIZED CONSENT PROVIDER STATEMENT:

I have explained this study and have offered the study participant an opportunity for any further discussion or clarification.

_____ _____ _____
NAME (PLEASE PRINT) CREDENTIALS PHONE NUMBER

_____ _____ _____
SIGNATURE DATE TIME