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PRINCIPAL INVESTIGATOR: Kangmin Zhu, Ph.D.

CONTRACTING ORGANIZATION: Meharry Medical College
Nashville, Tennessee 37208

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Nashville, Tennessee 37208

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This project has been extended because of the extra work proposed in our last report and because of the additional procedures for the enrollment of study women. This report covers the period from September 1, 1997 to August 31, 1998. During this period, the research team has made tremendous efforts for reaching the project goal. We have identified and interviewed with most cases and controls according to the sample size expected in the study design. We are collecting breast cancer tissue specimens from hospitals in the three counties where cases were pathologically diagnosed. These tissue specimens are being processed and stained for ER measurements. We have established and maintained the databases for administrative data, questionnaire data and tissue collection/measurement data. A hypothesis article based on the recent progress in molecular biology will be published soon. More efforts are being made to finish the project during the extended period.

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FOREWORD

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Kaufman-Zhu 9/18/98

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TABLE OF CONTENTS

INTRODUCTION

This is a report of our case-control study that aims to examine whether risk factor profiles of breast cancer differ according to the estrogen receptor (ER) status among African-American women ages 20-64. The past year was the second year, also the final year of the project, according to the original proposal. Because of the extra work proposed in our last report and because of new procedures undertaken in the past year to overcome barriers to the recruitment of study women, we need more time for the data collection activities. As a result, we applied for an extension of the project which has been approved. This extension is important for the study quality and the accuracy of future study results. This report, therefore, serves as an annual report covering the period from September 1, 1997 to August 31, 1998.

The extra work proposed in our last report include:

- Increasing the pool of patients by recruiting patients diagnosed in 1997;
- Collecting tumor tissue specimens and measuring ER status of tumors.

The new procedures to reduce barriers to the enrollment of study women primarily include:

- Increasing telephone calls and sending faxes to doctors who did not respond;
- Visiting homes of patients in the three counties who did not respond to the study after two mails and several reminder calls.

With very limited budget and personnel, the research team has made tremendous efforts for reaching the project goal and has worked on:

- Interviews with 168 cases;
- Random digit telephone dialing to select controls;
- Interviews with 131 controls;
- Sending oral contraceptive forms to cases and controls;
- Mailing paychecks to study subjects who participated in the study;
- Visiting patients who did not respond;
- Formulating procedures and establishing collaborations with hospitals for tissue collection;
- Collecting, processing and staining 82 tissue specimens for ER measurements;
- Establishing and maintaining the databases for administrative data, questionnaire data and tissue collection data;
- Entering into computer data that have been collected;
- An article that will be published in November (appendix 1).

The body of this report below summarizes the primary work we have finished up to August 31, 1998.

BODY

1. Overview of the study design

Estrogen-related factors, such as nulliparity, age at first full-term pregnancy, age at

menarche, and age at menopause, are known to be risk factors for breast cancer. Because estrogen executes its influence on the biological activity and growth rate of breast cells through hormone receptors, whether these factors can increase the risk of breast cancer may depend upon the existence of estrogen receptors. This study uses a case-control design to examine whether risk factor profiles are different between ER-positive and ER-negative tumors among African-American women. Cases consist of about 200 African-American female patients diagnosed with breast cancer during 1995-97 and who were aged 20-64 and lived in Davidson, Shelby and Hamilton counties, Tennessee. All breast cancer patients were histologically confirmed and identified through Tennessee Cancer Reporting System (TCRS). Controls are comprised of African-American women without breast cancer who are selected through random-digit telephone dialing and frequency matched to cases by 5-year age range. Information on risk factors is collected through telephone interviews. Tumor tissue samples are collected for the determination of estrogen receptor status. In addition, a set of colored pictures of oral contraceptive (OC) pills and a short OC questionnaire are mailed to the study subjects with the pay check to collect detailed information about OC use. Risk factors for breast cancer will be analyzed according to ER status of tumors.

2. Doctors' consent

We quarterly obtain a list of patients from TCRS. We link the patient data with physicians' database provided by TCRS and then mail the doctors a letter and a consent form. The letter we send describes the study and asks if we can contact their patients. If a physician does not return the consent form after two mails, one of our staff members makes a call to the

physician's office to determine the status of the letter and fax or mail another copy of the letter and consent form when needed. Because of the difficulties in reaching some doctors, we decided to make more calls or send faxes to contact the doctors. Although unsuccessful, we have also made other efforts to increase doctors' response rate, such as soliciting a cover letter from influential people for our mails to doctors and visiting some doctors who did not give us consent for all of their patients.

In the five waves of data with which we have completed work, TCRS provided us 516 eligible patients with breast cancer. Out of the patients, 98 had no doctors identified and 14 died. Two hundred and thirty-two doctors were identified for the remaining 404 patients and were contacted. Table 1 summarizes doctors' responses to our letters and remind calls.

Overall, 83.6% of doctors (n=194) responded to our study with the number of 319 patients (79.0% of all patients with a doctor identified). For these patients, doctor's consent was obtained for 270 of them (84.6%).

Table 1. Doctors' responses according to the first mailing, second mailing and reminder call

	Doctor not responded	Doctor responded	Status of patients with doctor's response		
			Agreed to contact	Refused to contact	Patient died
1st mail	141*	91*	166**	5**	5**
2nd Mail	110	31	39	15	2
Reminder call(s)	38	72	65	100***	7

*, number of doctors; **, number of patients, *** Including patients with doctors who did not want to be involved in the study at all.

Contacting doctors of the 6th wave patients is underway. We have obtained the consent from 11 out of 20 doctors up to August 31st.

3. Recruitment of eligible patients

After obtaining doctor's consent, we sent patients a packet including a cover letter introducing the study and a consent form for their participation in the study. The second letter is sent to those who did not respond to the first one. A reminder call (where a telephone is available) is made to women who did not reply to both mailings. Table 2 shows the outcomes of our first and second mailings and reminder calls to the first five waves of patients.

Table 2. Patients' responses according to the first mail, second mail and reminder call

	Women responded		Women not responded		Total
	Agreed to participate	Refused to participate	Unable to locate	Other	
1st mail	45	1	5	219	270
2nd Mail	40	0	0	179	219
Reminder call	30	6	10	29	75*

*, the number of patients with a telephone number available.

Among patients to whom we contacted, the percentages of women who agreed and refused to participate in the study were 42.6 and 2.6, respectively. The rest of them either did not respond to the study or could not be located.

It is known that African-Americans are less likely to participate in clinical trials or other studies [1,2]. Although we paid participants for their time for the study and provided them with an opportunity to win $200 and although we have used an intensive procedures to get their responses, the participation rate of eligible women was still lower than we expected.

Having recognized that some non-responses may result from the ignorance mails, the lack of understanding the importance of the study, or the mistrust of the medical system, we

added a component of home visits. We send a nurse, a breast cancer survivor, a social worker, or a research team member of African-American ethnicity to non-respondents' homes to get their consent by reducing the barriers to their participation. Our current data showed that the participation rate is much higher for home visits: 81.5 percent of women we could talk to agreed to participate (table 3). However, a substantial number of women have moved or died because patients were identified through the cancer registry and available for our study at least half-one year after their diagnosis and because subjects include patients diagnosed 2-3 years ago.

Table 3. Home visits to women who did not respond to the study and the outcomes

# Homes visited	107
# Women whom we were able to talk to	65
# consents	53
# Refusals	11
# Poor health status	1
# Women whom we were unable to talk to	42
# Died	10
# Moved	17
# Unknowns	5
# Miscellaneous	10

We currently have 10 patients from the 6th wave who have a doctor's consent for us to

contact. We have gotten 2 cases from this wave who agreed to participate. Up to August 31, 168 patients have been interviewed and therefore included in the case group.

4. Selection of controls

Controls are selected using random digit dialing techniques, and frequency matched to cases by 5-year age range. First, we group cases diagnosed in the same calendar year whose telephone area codes and prefixes serve the same residence area, and form the sampling frame by age distribution of the cases in the area. Then, we randomly select one of the telephone prefixes of the cases and adding the last four random-selected digits to constitute a telephone number. A call to this number is made to find an eligible woman according to ethnic background and age range. Up to 9 calls over a two week period, including 3 day-time, 3 evening, and 3 weekend calls, are made for a telephone number that has not answered. If an eligible woman is identified, we describe the study purposes and procedures, mention monetary incentives of $25 for an interview and a drawing for $200, and ask whether she would accept a telephone interview. For a woman who agrees to participate, a telephone interview is conducted.

Up to August 31st, 1998, we have called 7,747 random-digit telephone numbers and identified 183 eligible women. Seventy-two percent of these women (n=131) have given us consent and have been interviewed.

5. Oral contraceptive forms

We mailed to interviewed cases and controls a set of colored pictures of oral contraceptive (OC) pills and a short OC questionnaire with a paycheck. For those who did not return a completed OC questionnaire, we sent another set OC pill pictures and questionnaire. Currently, 82 of cases (48.8%) and 49 of controls (37.4%) returned a completed OC questionnaire to us.

6. Tumor tissue collection and processing

Up to now, we have requested 140 tumor tissue specimens from 16 hospitals in the three counties. The tissue specimens are picked up by our research staff or shipped to us by the hospitals. They are returned to the hospitals after we make tissue slides. To maintain good cooperative relationship with the hospitals, we give a thanks letter with each tissue specimen returned. Out of 140 specimens requested, we have already obtained 82 (58.6%). More specimens are being obtained. The collected specimens have been processed and stained, and will be read for the determination of ER status. Tumor tissue collection, processing, staining and reading are being continued.

7. Recommendations in relation to the statement of work

As stated in the Introduction and Conclusions, we have applied for an extension of the project for 6 months.

CONCLUSIONS

According to the statement of work in the original proposal, this project should be finished on August 31, 1998. However, we had to apply an extension for data collection based on the following reasons. First, the research team was unable to be fully staffed until May 1997 due to Meharry's procedures for hiring staff. The remaining period of slightly more than one year is not enough to complete all subjects identifications, interviews, data entry, data cleaning and analysis and writing a final report for such a population study. Second, as we mentioned in our last report, we need to recruit patients diagnosed in 1997 to get more cases. Because patients identified through the cancer reporting system are not available to us at least 6 months after their diagnosis, we need extra time to obtain them. Third, also as we proposed in our last report, we would measure ER status in our laboratory instead of using pathological reports from different hospitals. Collecting, storing, processing and measuring tumor tissue specimens entail wide collaborations from all involved hospitals and from people in basic sciences and pathology. Finally, because of the barriers to the enrollment of eligible women into a study, we had to visit homes of eligible women who did not respond to the study to increase the participation rate. Such home visits involve all three counties – Davidson County (Nashville area), Shelby County (Memphis area) and Hamilton County (Chattanooga area), and therefore have greatly increased our working load. The extra work mentioned here is necessary for improving the study quality and therefore the accuracy of future results. This is important because there have been no studies among African-American women on the study topic.

To reach the study goal, the research team has been struggling to overcome three major difficulties: (1) very limited budget (an annual direct costs of about $52,250 from DOD), (2) shortage of project staff due to limited budget, and (3) much more work to get an eligible woman, compared with a study in the majority population (such as difficulties in finding a control using RDD). Despite these difficulties, we have already interviewed 168 cases and 131 controls and collected 82 tumor tissue specimens (more specimens are being collected). The number of cases is close to that expected in the proposal. The participation rate of eligible women has been increased from 42.6% before home visits to 62.2% after home visits. Although not very satisfactory yet, the increase will substantially improve the validity of the study. Moreover, we have already had a forthcoming publication that reviews the potential problems in studies in terms of ER status and raises a new study hypothesis based on the recent molecular development. Considering such limited resources (budget and personnel), such big working load and additional difficulties for a minority institution and for recruiting minority study subjects, our research team, especially our project coordinator, Sandra Hunter, has done an excellent job.

We applied for an extension of 6 months that has been approved. During the period, we will have a lot of work to do especially in identifying and enrolling controls through RDD, tissue collection and ER measurement, data entering/cleaning/editing, and data analysis (we do not have a data analyst currently and therefore the P.I. will assume the work). We will continue trying our utmost to overcome various obstacles and reach our project goal.

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APPENDICE

The acceptance letter of the article to be published in November, 1998

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Harvard School of Public Health
677 Huntington Ave., Boston MA 02115, USA
Tel (617) 432 4595 Fax (617) 734 4713
Email jkwalsh@sph.harvard.edu

To: Author(s) Zhu et al.

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Graham A. Colditz, MD, DrPH
Editor
Cancer Causes & Control
Channing Laboratory
181 Longwood Avenue
Boston, MA 02115
Telephone: (617) 525-2258
Fax: (617) 525-2008

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