

AD _____

GRANT NUMBER DAMD17-94-J-4255

TITLE: Magnetic Fields and Breast Cancer Risk

PRINCIPAL INVESTIGATOR: Doctor John Peters

CONTRACTING ORGANIZATION: University of Southern California
Los Angeles, California 90033

REPORT DATE: October 1997

TYPE OF REPORT: Annual

PREPARED FOR: Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

19980130 165

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE October 1997	3. REPORT TYPE AND DATES COVERED Annual (30 Sep 96 - 29 Sep 97)	
4. TITLE AND SUBTITLE Magnetic Fields and Breast Cancer Risk		5. FUNDING NUMBERS DAMD17-94-J-4255	
6. AUTHOR(S) Doctor John Peters		8. PERFORMING ORGANIZATION REPORT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Southern California Los Angeles, California 90033			
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Commander U.S. Army Medical Research and Materiel Command Fort Detrick, Frederick, Maryland 21702-5012		10. SPONSORING/MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES			
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited		12b. DISTRIBUTION CODE	
<p>13. ABSTRACT (Maximum 200)</p> <p>We will begin the final year of data collection on a nested case-control study of the association between magnetic field and breast cancer risk among a group of predominantly African-American and Latino women in Los Angeles County. The research questions remain as follows:</p> <p><u>Primary</u></p> <p>1.) Is residential exposure to magnetic fields, as assessed by wiring configuration coding in homes occupied over the past 10 years before diagnosis, associated with the risk of breast cancer. Wiring configuration coding is a method that uses data on the types and distances to nearby outdoor electrical wiring to impute magnetic field levels in homes.</p> <p>2.) Do higher exposures to alternating current (AC) magnetic fields, as assessed by 7 days of measurements, increase a woman's risk of breast cancer.</p> <p><u>Secondary</u></p> <p>1.) Do particular combinations of the alternating current (AC) magnetic field and the direct current (DC) magnetic field, increase the risk of breast cancer. The AC field results from our use of the 60 Hz electric power supplied by utilities; the DC (or static) field results from the earth's magnetic field but is altered by the environment within residences. This hypothesis was prompted by observations of biologic effects at particular combinations of the AC and DC fields in several experimental systems.</p>			
14. SUBJECT TERMS Breast Cancer, Magnetic Fields, Residential History, African-American and Latina Women.		15. NUMBER OF PAGES 10	
17. SECURITY CLASSIFICATION OF REPORT Unclassified		16. PRICE CODE	
		20. LIMITATION OF ABSTRACT Unlimited	
18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

____ Where copyrighted material is quoted, permission has been obtained to use such material.

____ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

____ Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

____ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

____ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

____ In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.


PI - Signature

10-21-97
Date

Table of Contents

Front Cover	page 1
SF 298 Report	page 2
Foreword	page 3
Table of Contents	page 4
Introduction	pages 5-6
Body of Report	pages 6-8
Conclusion	page 8
References	pages 9-10

INTRODUCTION

Primary Specific Aims:

1. One primary specific aim is to determine if residential exposure to magnetic fields, as assessed by wiring configuration coding, is associated with the risk of breast cancer. Wiring configuration coding is a method that uses data on the types and distances to nearby outdoor electrical wiring to impute magnetic field levels in homes. Specifically, we will test whether subjects who have lived over the past 10 years in homes with wiring configurations associated with higher exposure to magnetic fields have an increased risk of breast cancer.
2. Another primary specific aim is to determine whether higher exposures to alternating current (AC) magnetic fields, as assessed by 7 days of measurements, increase a woman's risk of breast cancer. Measurements will include 6 days of measurements in the bedroom of the current residence and 1 day of personal monitoring.

Secondary Specific Aim:

1. The secondary specific aim is to test the hypothesis that particular combinations of the alternating current (AC) magnetic field and the direct current (DC) magnetic field, increase the risk of breast cancer. The AC field results from our use of the 60 Hz electric power supplied by utilities; the DC (or static) field results from the earth's magnetic field but is altered by the environment within residences. This hypothesis was prompted by observations of biologic effects at particular combinations of the AC and DC fields in several experimental systems. In year two we received supplementary funding from the ARMY to update our exposure assessment protocol to better address this hypothesis. We now use the Multiwave System II to simultaneously make the spot measurements of the AC and DC fields so that we can be sure of their relative orientations.

Significance:

Major differences in breast cancer rates between low incidence countries in Africa and Asia and high incidence countries in Northern Europe and North America (Parkin 1992), as well as the rise in incidence over time (Devesa et al., 1987), suggest that some correlate of industrialization influences breast cancer risk. Although many factors correlate with industrialization, including changing reproductive patterns, increasing exposure to magnetic fields produced by the electric power system could play a role (Stevens et al., 1992). Support for this conjecture comes from the laboratory in the form of a plausible biologic mechanism linking EMF exposure to enhanced risk of breast cancer (Stevens et al., 1992). Central to the hypothesis are laboratory studies of the effects of magnetic field exposure on pineal function, in particular melatonin production (Kato et al, 1993), and the inhibitory effects of melatonin on mammary carcinogenesis (Hill and Blask, 1988). Melatonin, a hormone crucial to regulation of circadian rhythms, also plays a role in control of the reproductive cycle (Tamarkin et al., 1985). In addition, more recent data suggest that magnetic field exposure, at levels close to those observed in homes, may decrease melatonin's inhibitory action on breast carcinogenesis (Liburdy et al., 1993).

While epidemiologic data are sparse, there is evidence that occupational exposure to magnetic fields, as approximated by job title, is a risk factor for breast cancer in both men (Matanowski et al., 1991; Tynes and Andersen, 1991) and women (Savitz and Loomis, 1994, Coogan et al., 1996). Further, there is data that female breast cancer risk is associated with higher residential exposure as assessed indirectly by wiring configuration coding (Wertheimer and Leeper, 1987)

There are laboratory and theoretical data that suggest that certain combinations of AC (time varying) and DC (static) magnetic fields may have enhanced potential for causing biological effects (Blackman and Most, 1993). These are generally referred to as magnetic-resonance hypotheses. While there are few epidemiologic data suitable for examining these hypotheses in relation to cancer risk, one recent study suggests that combinations of the AC and dc field are associated with the risk of childhood leukemia in Los Angeles (Bowman et al., 1995). Because of this exciting result, we included measurements of dc magnetic field in the home to address secondary aim # 2 above.

Methods of approach:

This is a nested case-control study. The base population is a cohort study of African-American and Latino women in Los Angeles County. Exposure assessment is by means of wire configuration coding combined with direct measurements of AC and DC magnetic fields. More detail is found in the Body of this report.

BODY OF THE REPORT

The study is funded by the ARMY for 4 years, we are presently nearing the end of year three of data collection. There are essentially no changes in the study methods over that proposed in the original submission with the exception of the fact that we received supplementary funding from the ARMY breast cancer program through the National Action Plan on Breast Cancer. This supplementary funding was to enable us to purchase the Multiwave System II exposure meter for making simultaneous spot measurements of the AC and DC fields to provide a more accurate test of our secondary hypothesis. In this study, we are assessing exposure to magnetic fields in three ways:

1. **Wiring configuration coding**, in which data on the types and distances to nearby outdoor electrical wiring (i.e.: transmission and distribution lines) are used to impute magnetic field levels in all homes in Southern California occupied by subjects in the past 10 years. We are using a protocol developed for an NCI funded study of childhood leukemia which has been extensively tested. This is a modification of the Wertheimer Leeper wiring configuration which has been associated with the risk of childhood cancer in a number of studies (Wertheimer and Leeper, 1979) but has not been well studied in relation to breast cancer. Wire coding involves drawing a map of the type of power lines running within 150 ft of the house and their distance from the house (250 for transmission lines). The wire coding is being done in a blinded fashion a computer algorithm after specified data are abstracted from the map.

2. **Direct recordings of alternating current (AC) magnetic fields** in the home over 7 days using Emdex magnetic field meters (Enertech Consultants, Campbell CA). The meter takes measurement every 120 seconds. The meter is worn by the subject for the first day and then placed at the bedside. After recording, we download the data to a laptop computer, check and then store the data for analysis.
3. **DC (static) magnetic field measurements** at several locations in the home using the Multiwave System II (ERM, State College PA). These are made along with corresponding spot measurements of the AC magnetic field at three locations in the bedroom (2 locations on the bed--where the subjects' head lies and where the chest lies), as well as in the bathroom, kitchen and living room. The use of Multiwave System II, which we were able to purchase thanks to supplementary funding from the ARMY enables these AC and DC spot measurements to be made simultaneously by the same instrument. This way we are certain of their relative orientation which is important to testing the secondary hypothesis.

A questionnaire regarding residential history and sources of magnetic field exposure at home (such as appliances) as well as history of occupational exposure to magnetic fields and exposure to light at night (a potential confounder) is also administered. The questionnaire was based largely on a questionnaire used in a recently completed study of magnetic fields and breast cancer in Seattle (NCI funded). However, we benefited from feedback from those investigators regarding which questions on their questionnaire did work as well as others.

The study is a case-control study nested within a cohort study of risk factors for breast and other cancers among African-Americans and Latinos in Los Angeles County directed by Dr. Brian Henderson . The cohort study is funded by the National Cancer Institute (CA 54281 – Lawrence Kolonel Principal Investigator). The base population for the nested case-control study consists of the cohort of approximately 74,000 women who are predominately Latino and African-American aged 45-74 years who responded to a 26-page mailed questionnaire which includes information on known risk and suspected risk factors for breast cancer and a detailed dietary history. The cohort was recruited from computer files of the Department of Motor Vehicles (for persons under age 65) and the Health Care Financing Administration (for persons over age 65). The nested case-control study of magnetic fields and breast cancer includes all incident cases of female breast cancer diagnosed within the cohort over 4 years. Women with incident breast cancer are identified through the population based tumor registry for Los Angeles County. Controls are a random sample of women in the cohort who do not have breast cancer. The review of first previous annual report expressed concern over the possibility that some of the controls might really have breast cancer. It is possible that a small number of women, were they subject of mammography, might have breast cancer. However, given the low annual incidence of breast cancer among women as a whole in this age group, we would predict that only a handful of women in the group of over 1000 controls will have breast cancer. This is clearly a trivial form of bias. This potential bias is minimized further because we will know whether a woman previously enrolled as a control is subsequently diagnosed. So, we can use the appropriate analytic techniques from the literature to deal with this handful of subjects. We have just recently expanded the base population to include women who self-report being non-hispanic white in the cohort who were recruited from the neighborhoods which were identified as predominately Latino. The reason is to ensure enrollment of our target number of cases and controls. The study population remains primarily minority women.

Cases and controls are contacted to participate in the measurements and questionnaire. Women who chose not to take the time to actively participate in measurements can be included because exposure can be indirectly assessed by wire configuration coding the home occupied at the time of diagnosis. In addition, data on risk factors for breast cancer are available on all subjects from the baseline cohort study questionnaire.

Quality control:

Emdex meters and magnetometers are formally factory calibrated every 6 months but we calibrate the weekly at the office using equipment designed by our engineering consultant, William Kaune, and thus would identify any faulty machines (no problems to date). Wire coding is done blind to case or control status. Wire coders were trained by William Kaune and adhere to a standard protocol for drawing maps. The actual wire code is assigned by a computer algorithm to eliminate potential bias. Dr. Kaune has designed a calibration unit for the Multiwaves and we calibrate weekly. We will also send the Multiwaves to the factory for calibration yearly. Quality control for wire code entails having a random sample of wire maps redrawn by an experienced mapper, Bob Workley with Eneritech Consultants. He did all wire coding for the large NCI funded study of childhood leukemia published this year. We then compare these maps to those of our study mappers and identify any discrepancies and discuss them while at the location. This will be repeated every 6 months. To date we have had excellent concordance. The only minor discrepancies have involved the parameter of thick versus thin wires which is a known weakness of the original Wertheimer Leeper wire code as it is subjective. However, we also use the modified Kaune code which does not use this parameter.

Study progress:

The study is jointly funded by NIEHS (grant number 5 RO1 ES 06912) and is a five year study with the fifth year funded by NIEHS after the four years of ARMY funding conclude. This first year was devoted to setting up all study protocols and pilot testing and then finalizing the protocols in the field. During the second year we altered the protocol to include the Multiwave System II meters for spot measurements based on the supplementary funding we received from the ARMY. Because of the long-term nature of this project, we are not able to present results at this time. We have completed interviews and home measurements for 191 cases and 174 controls. We have drawn wire maps for at least one residence on 216 cases and 230 controls. We have partial participation for an additional 18 cases and 34 controls. Participation rates are at the level we had predicted in the original submission which is substantially better than standard population based case-control studies in this ethnic mix. This is a benefit of the nested case-control study design. The average subject has lived in the residence in which we make measurements for 22 years and 76% of subjects occupied only one residence for the past 10 years. Only 8 subjects have had a residence in the past 10 years outside of Southern California and thus cannot be mapped. Map and questionnaire data have been keyed on all subjects enrolled. We have examined the distribution of wire codes among the subjects enrolled and are reassured to find that it is quite similar to that obtained in earlier studies we have done in Los Angeles County.

CONCLUSION

Epidemiologic studies of this type take time to complete. We are not yet able to draw conclusions. It would be extremely misleading to do preliminary case-control analyses and it could bias the future data collection.

REFERENCES

Blackman CF, Most B (1993): A Scheme for Incorporating DC Magnetic Fields into Epidemiological Studies of EMF Exposure. *Bioelectromagnetics* 14:413-51.

Bowman JD, Thomas DC, London SJ, Peters JM (1995): Hypothesis: The risk of childhood leukemia is related to combinations of power-frequency and static magnetic fields. *Bioelectromagnetics* 16:48-59.

Cougan PF, Clapp RW, Newcomb PA, et al. Occupational Exposure to 60-Hertz magnetic fields and risk of breast cancer in women. *Epidemiology* 1996;7:459-464.

Devesa SS, Silverman DT, Young JL, Pollack ES, Brown CC, Horm JW, Percy CL, Myers MH, McKay FW, Fraumeni JF (1987): *JNCI* 79:701-770.

Hill SM, Blask DE (1988): Effects of Pineal Hormone Melatonin on the Proliferation and Morphological Characteristics of Human Breast Cancer Cells (MCF-7) in Culture. *Cancer Res* 48: 6121-6126.

Kato M, Honma K, Shigemitsu T, Shiga Y (1993): Effects of Exposure to a Circularly Polarized 50-Hz Magnetic Field on Plasma and Pineal Melatonin Levels in Rats. *Bioelectromagnetics* 14: 97-106.

Lednev VV (1991): Possible mechanism for influence of weak magnetic fields on biological systems. *Bioelectromagnetics* 12:71-76.

Liburdy RP, Sloma TR, Sokolic R, Yaswen P (1993): ELF Magnetic fields, Breast Cancer, and Melatonin: 60 Hz Field Block Melatonin's Oncostatic Action on ER+ Breast Cancer Cell Proliferation. *J. Pineal Res* 14: 89-97.

Loomis DP, Savitz DA, Ananth CV (1994): Breast cancer mortality among female electrical workers in the United States. *J Natl Cancer Inst* 12:921-925.

Matanoski GM, Breyse PN, Elliot EA (1991): Electromagnetic Field Exposure and Male Breast Cancer. *Lancet* 337: 737. (letter to the editor).

Parkin DM, Muir CS, Whelan SL, Gao YT, Ferlay J, Powell J (1992): Cancer Incidence in Five Continents. IARC Scientific Publications NO. 120. Lyon, France: International Agency for Research on Cancer.

Stevens RG, Davis S, Thomas D, Anderson LE, Wilson BW (1992): Electric power, pineal function and the risk of breast cancer. *FASEB Journal* 6: 853-860.

Tamarkin L, Baird CJ, Almeida OFX (1985): Melatonin: a coordinating signal for mammalian reproduction. *Science* 227:714-720.

Tynes T, Andersen A (1990): Electromagnetic Fields and Male Breast Cancer. *Lancet* 336: 1596 (letter to the editor).

Wertheimer N, Leeper E (1979): Electrical wiring configurations and childhood cancer. *Am J Epidemiol* 109:273-84.

Wertheimer N, Leeper E (1987): Magnetic Field Exposure Related to Cancer Subtypes. *Annals New York Academy of Sciences* 502: 43-53.