Mr. BURTON. Thank you, Ms. Silver.

Dr. Beilin and Dr. Trimble, we will be back in just a few minutes. We have one vote on the floor. I am anxious to hear from both of you, so we will be right back.

[Recess.]

Mr. BURTON. I want to first of all thank you for your patience. This has been a very, very long day. I am a little disappointed that what you are going to tell us is probably very, very significant and we didn't have you on earlier in the program. Nevertheless, I can assure you that what you tell us today will be taken to heart and used, and we will talk to the various agencies about it.

So let's start, I guess go down the list with you, Dr. Beilin.

Dr. BEILIN. OK. Thank you very much, Mr. Chairman, and members of the committee. Thank you for the opportunity to be here today. My name is Dr. Dan Beilin, OMD, LAc. I have a doctorate in herbal and oriental medicine, and hold a degree in physiology, as I was physiologist at the UCLA Department of Gastroenterology. I am in private practice in California in European complementary medicine and oriental medicine. I have been working in cooperation with a group of doctors and a radiologist, who have been measuring changes in the skin and the nervous system of patients who develop devastating diseases, such as cancer and autoimmune disorders. We have found a high correspondence between the nervous system's ability to control metabolism and circulation, also referred to as thermoregulation or heat regulation, and the growth of tumors and other degenerative disorders.

In complementary medicine, we try to step back one step and view the patient in terms of the interactions between the internal organs and tissues. Traditional orthodox medicine too often focuses on a single organ of the body, when in reality, many organs are involved in a subtle or not-so-subtle manner in the advancement of a particular disease state. Yet when we look at the body as a collection of systems, each interrelated with the others, we can actually begin to search for the cause of illness. Fortunately, I believe that we are approaching a technology which will provide a bird's eye view of the body as a whole, providing information about multiple organ expression and painting a picture of biological processes that may bring us closer to finding the cause of such diseases as breast cancer.

One technology is called regulation thermography, developed in Germany and legally marketed in the United States now. Regulation thermography offers a serious addition to the arsenal of physicians evaluating patients at risk of cancer or cancer recurrence. It works by taking temperature measurements of neurologically controlled points on the skin often above the organ in question, stressing the body with cool air, and then taking a second measurement of the same points. Computer software analyzes the response of the points and their adaptation to the rapid temperature change. More than 25 years of experience has demonstrated a relationship between such responses in organ pathology. The test is non-invasive, painless, and the machine is small enough to fit into a briefcase.

Regulation thermography is not intended to be a substitute for mammography or other methods of cancer detection. What it does do is provide information to the practitioner about the environment

in the body that could be contributing to the cancer growth, allowing the practitioner to design a treatment strategy utilizing the principles of alternative and complementary medicine, staying within the constraints of good science.

I prepared a few slides that better illustrate the theory behind regulation thermography and its contribution to cancer detection and treatment. So if you will check the monitors, the first slide is the idea of terrain versus tumor. Here, we see a large box, which represents healthy cells and fluids of the body. The small box represents a tumor which has grown for some reason and has now been diagnosed say by a mammogram. Medicine as of 1999, today, has given special attention to the destruction of the tumor, whether by surgery, chemotherapy, or radiation, but has neglected the internal environment that has contributed to the development of that tumor. Until recently, there have not been scientifically verifiable methods for measuring the factors in that tumor terrain. But this is critical if we are to develop therapeutic approaches aimed at treating the whole patient, not simply mounting a frontal attack on the tumor alone.

The second slide illustrates how we are internally wired, that the internal organs, such as the stomach, pancreas, liver or prostate, are capable of talking to the nervous system by taking precise measurements of skin temperature as we stress the body, similar to a stress ECG by the cardiologist, we can see how the organs and other tissues of the body behave around that stress. Changes in the way the body behaves to stress can indicate the possible presences of pathologies or pre-pathologies. German and Swiss researchers have gathered data over the last 20 years which have established normal values for stress reactivity in every skin region. Furthermore, many disease states have been documented for their patterns of skin dysfunction over the whole body.

Mr. Chairman, this is a method that is objective, reproducible, and very serious consideration for inclusion into every new complementary medicine hospital and program. It measures the pattern of response to stress which takes place in the terrain of the body. The information gathered can act as a marker test for lifestyle change prescription effect and preventive measures that have the potential to cut the increasing cost of cancer care.

In slide three, we see a thermogram above done with this new technology. Above, a normal thermogram, and below, a chaotic thermogram. You can see how there is a complete disruption of a certain pattern. The top one looking homogeneous, the next looks mixed up, showing a lack of regulation, of homeostasis or balance by the organs and nervous system. This is the whole body, with data taken from 80 points.

In the next slide, this is a study done by Professor Wagner in Germany. We see this, that 63 patients on the left bar with confirmed breast cancer by pathology, were sent to blind doctors doing clinical exams alone, with mammography added, and then with regulation thermography in conjunction with mammography. Interestingly, a higher percentage of tumors were identified using regulation thermography in conjunction with mammography than with mammography alone.

This and other studies conducted in Europe demonstrate that dynamic thermography can be a valuable tool in helping to diagnose the presence of occult disease. In fact, some studies suggest that in some cases, regulation thermography offers a viable alternative to mammography. If proven true, this would particularly be useful in geographic regions lacking mammography facilities or as a preliminary screening device for the family physician. In addition, studies suggest that regulation thermography may be able to detect the changes in the body that may preface the development of cancer. With regard to breast cancer and other types of tumors, research indicates that most tumors have taken at least 5 years from their inception to develop into a viewable size. What has occurred to the body's immune mechanisms during those years which creates the pre-tumor and then tumor? What do we know about the fertility of our inner soil, if you will, which nourishes or depletes the development of tumors? For these reasons, I strongly urge consideration for funding for studies in the United States.

On the last slide, of course breast cancer is not the only disease for which this technology may be utilized. Here is a statistical average of three patients with a progression of PSAs used as a prostate marker, and their corresponding thermogram of the prostate points taken by this method. Note the correspondence of a higher PSA, say on the left is 12.53, to the higher degree of rigidity of response seen in the thermogram are quite evident. When we see the lowering of the PSA, we see a better thermograph coming out as a result.

The point I make is that complementary medicine is not only comprised of non-scientifically based methods. It has in the past been shunned from the mainstream, but the effect has been to throw the baby out with the bath water. In recent years, Congress has taken important steps to address this issue, primarily through the creation of the Center for Alternative Medicine at the NIH, and the provision of increased funding for research in alternative medicine. Many leading teaching hospitals and other medical centers have established programs focused on researching and using alternative and complementary therapy. One of the roles for the Center of Alternative Medicine should be to act to bring these integrative centers together for advanced research on key technology, such as regulation thermography, and to provide additional funding for research so that the valuable alternative therapies will assume their proper place within the entire healthcare system.

Finally in closing, I also recognize that Congress this year will be dealing with the critical issue of patient rights with regard to Government funded and private healthcare plans. Unfortunately, alternative medicine has been neglected in the coverage decision-making of many healthcare programs. I ask you while considering this critical legislation, to keep in mind the proven benefits of alternative medicine, and the desires of a significant portion of the American public to have access to such treatment.

Thank you, Mr. Chairman, for inviting me here today. I appreciate this wonderful opportunity to share my opinions regarding present and future trends in medicine. I hope we can work together in the future.

[The prepared statement of Dr. Beilin follows:]

Statement of

Daniel Beilin, OMD

Before the

Committee on Government Reform

U.S. House of Representatives

On

Regulation Thermography and the Role Of Complementary and Alternative Medicine In Cancer Treatment and Prevention

June 10, 1999

Daniel Beilin, OMD,
Lecturer, Researcher,
Founder, American Academy for Regulation Thermography (AART)
Private Practice, Oriental and Complementary Medicine
9057 Soquel Dr. Ste. A-B
Aptos, California, 95003
Tel: (831) 685-1142
Fax: (831 685 1128
Email: **dbeilin@got.net**

Mr. Chairman, members of the committee, thank you very much for the opportunity to be here today. My name is Daniel Beilin, OMD, L.Ac. I have a doctorate in Herbal and Oriental Medicine, and hold a degree in physiology, as I was chief physiologist at the UCLA Department of Gastroenterology. I am in private practice in Oriental and European Complementary Medicine. Recently I have been working in cooperation with a group of doctors and a radiologist who have been measuring changes in the skin and nervous system of patients who develop devastating diseases such as cancer and autoimmune disorders. We have found a high correspondence between the nervous system's ability to control metabolism and circulation, also referred to as thermoregulation (or heat regulation), and the growth of tumors and other degenerative disorders.

In complementary medicine, we try to step back one step and view the patient in terms of the interactions *between* his internal organs and tissues. Traditional, orthodox medicine too often focuses on a single organ of the body, when in reality many organs are involved in a subtle or not so subtle manner in the advancement of a particular disease state. Yet only when we look at the body as a collection of systems, each interrelated with the others, can we actually begin to search for the cause of the illness. Fortunately, I believe that we are approaching a technology which will provide a bird's eye view of the body as a whole, providing information about multiple organ expression and painting a picture of biological processes that may bring us closer to finding the cause of such diseases such as breast cancer.

This technology is called Regulation Thermography. Developed in Germany and legally marketed in the United States, Regulation Thermography offers a serious addition to the arsenal of physicians evaluating patients at risk of cancer or cancer recurrence. It works by taking temperature measurements of neurologically-controlled points on the skin, often above the organ in question, then stressing the body with cool air, and then taking a second measurement of the same points. Computer software analyzes the response of the points in their adaptation to a rapid temperature change. More than 25 years of research has demonstrated a relationship between such responses and organ pathology. The test is a non-invasive and painless, and the machine is small enough to fit into a briefcase.

Regulation Thermography is not intended to be a substitute for mammography or other methods of cancer detection. What it does do is provide information to the practitioner about the environment in the body that could be contributing to the cancer growth, allowing the practitioner to design a treatment strategy utilizing the principles of alternative and complementary medicine, staying within the constraints of good science.

I have prepared a few slides that better illustrate the theory behind Regulation Thermography, and its contribution to cancer detection and treatment.

SLIDE 1: Terrain vs. Tumor

Here we see the large box, which represents the healthy cells and fluids of the body. The small box represents a tumor, which has grown and now has been diagnosed by a mammogram. Medicine, as of 1999, has given special attention to the destruction of the tumor, whether by surgery, chemotherapy or radiation, but has neglected the inner ENVIRONMENT that has contributed to the development of that tumor. Until recently, there have not been scientifically verifiable methods for measuring the factors in that tumor-terrain. But this is critical if we are to develop therapeutic approaches aimed at treating the whole patient, not simply mounting a frontal attack on the tumor.

SLIDE 2:

This slide illustrates how we are internally wired - that the internal organs such as the stomach, pancreas, liver or prostate, are capable of "talking" to the nervous system. By taking precise measurements of skin temperature as we stress the body - similar to a stress ECG - we can see how the organs and other tissues of the body behave around that stress. Changes in the way the body behaves to stress can indicate the possible presence of pathologies including cancer.

German and Swiss researchers have gathered data over the last 20 years which has established normal values for stress reactivity in every skin region. Furthermore, many disease-states have been documented for their patterns of skin dysfunction over the whole body.

Mr. Chairman, this is a method that is objective, reproducible and bears serious consideration for inclusion into every new complementary medicine hospital and program. It measures the pattern of response to stress, which takes place in the "terrain" of the body. The information gathered can act as a "marker test" for lifestyle change, prescription effect, and preventive measures that have the potential to cut the increasing cost of cancer care.

SLIDE 3

Here we see a thermogram done with this new technology: Above, a normal thermogram, and below, a chaotic thermogram, typical of what you see in people with cancer. You see how one looks homogenous, and the next looks mixed-up, showing the lack of Regulation of Homeostasis by the organs and nervous system. This is the whole body, with data taken from 80 points.

SLIDE 4:

Here we see the research completed by Prof. G. Wagner in Germany.

63 patients with confirmed breast cancer by pathology, were sent to blinded doctors doing clinical exams alone, with mammography added, then with regulation thermography in conjunction with mammography. Interestingly, a higher percentage of tumors were identified using regulation thermography in conjunction with mammography, than with mammography alone. This and other studies conducted in Europe demonstrate that dynamic thermography can be a valuable tool in helping to diagnose the presence of occult disease. In fact, some studies even suggest that, in some cases, regulation thermography offer a viable alternative to mammography. If proven true, this would be particularly useful in geographic regions lacking mammography facilities, or as a preliminary screening device for the family physician. In addition, studies suggest that Regulation Thermography may be able to detect the changes in the body that may preface the development of cancer. With regard to breast cancer and also other types of tumors, research indicates that most tumors have taken at least 5 years from their inception to develop into a viewable size. What has occurred to the body's immune mechanisms during those years, which creates the pre-tumor and tumor? What do we know about the "fertility" of our inner soil if you will -which nourishes or depletes the development of a tumor?

For these reasons, I strongly urge consideration for funding for studies in the US.

SLIDE 5:

Of course, breast cancer is not the only disease for which this technology may be utilized. Here is a statistical average of 4 patients with progression of PSA's, and their corresponding thermogram of the prostate points. Note the correspondence is quite high. At this point, I don't think any urologist would turn down an additional prostate marking method, since the methods we have are insufficient or too aggressive.

The point I make is that complementary medicine is not only comprised of non-scientifically based methods. It has, in the past, been shunned from the mainstream, but the effect has been to throw the baby out with the bath water. In recent years, Congress has taken important steps to address this issue, primarily through the creation of the Center for Alternative Medicine at the NIH, and the provision of increased funding for research in alternative medicine. Many leading teaching hospitals and other medical centers have established programs focused on researching and using alternative and complementary therapies. One of the roles of the Center for Alternative Medicine should be to act to bring these Integrative Centers together for advanced research on key technologies, such Regulation Thermography, and to provide additional funding for research so that valuable alternative therapies will assume their proper place within the entire health care system.

Finally, in closing, I also recognize that Congress this year will be dealing with the critical issue of patient rights with regard to government funded and private health care plans. Unfortunately alternative medicine has often been neglected in the coverage decision making of many health care programs. I ask you while considering this critical legislation to keep in mind the proven benefits of alternative medicine and the desires of a significant portion of the American public to have access to such treatment.

Thank you, Mr. Chairman, for inviting me here today. I appreciate this wonderful opportunity to share my opinions regarding present future trends in medicine. I hope we can work together in the future.
-Dr. Beilin

Mr. BURTON. Dr. Beilin, before we go to Dr. Trimble, I hope when we get to the questions and the answers, that you will talk about, I think it was a proton device that can attack prostate cancer?

Dr. BEILIN. There is a type of hyperthermia that is a local hyperthermia device that is being reviewed right now.

Mr. BURTON. I want to ask you about that when we get to the questions and answers.

Dr. Trimble, thank you, sir, for being so patient with us today.

Dr. TRIMBLE. Chairman Burton, members of the Committee on Government Reform, thank you for inviting me to represent the National Cancer Institute at this hearing. I am head of the surgery section at the Division of Cancer Treatment and Diagnosis at the NCI. Sitting behind me today is Dr. Jeffrey White, who is Director of the NCI's Office of Complementary and Alternative Medicine.

By training, I am an obstetrician/gynecologist and gynecologic oncologist. My own patients include many women with cervical, uterine, ovarian, and breast cancer. My experiences in medicine as well as my own experiences caring for family members with cancer have made clear to me the importance of a holistic approach in cancer care.

The NCI is committed to fostering the integration of complementary and alternative medicine into modern cancer care. In 1989, we funded key research conducted by Dr. David Spiegel and his colleagues at Stanford and the University of California which demonstrated that psychosocial support prolonged long survival in women with metastatic brain cancer. Working with the National Center for Complementary and Alternative Medicine, we have established a cancer advisory panel for the National Cancer Institute. This panel, which meets three times a year, includes members from the conventional and the CAM cancer research community. This panel will help advise the NCI's Office of Complementary and Alternative Medicine run by Dr. White, on how best to evaluate CAM therapies, how to develop accurate CAM information for the public. We are also working with the National Center for Complementary and Alternative Medicine and other NIH institutes to establish centers for CAM research across the United States.

I would like to mention a few examples of the NCI's commitment to complementary and alternative approaches in cancer research. As Chairman Burton mentioned, for many years, the NCI has had a program evaluating natural products for anti-cancer activity. One of these products, Taxol, which is found in the bark of the Pacific yew tree, has been shown to improve survival significantly for women with breast, ovarian cancer. We have extended our study of natural products from plants to marine products. We are currently evaluating another natural product, shark cartilage, among patients with breast and lung cancer. We have evaluated chrono-biology, the delivery of chemotherapy timed to a person's circadian rhythms, in women with uterine cancer. We funded an important study conducted at the Harvard Medical School and published last week in the New England Journal of Medicine, which showed that new use of alternative medicine was a marker for greater psychosocial distress and worse quality of life in women with newly diagnosed breast cancer. We have started an unconventional innova-

tions program to spur the development of new technology in the diagnosis and treatment of cancer.

We have heard some discussion of the problems of lymphedema today. We have recently opened two phase III trials evaluating the safety of sentinel lymph node biopsy in women with breast cancer. If this is proved safe and efficacious, then we will be able to eliminate the need for axillary lymph node dissection, and spare these women the risk of lymphedema.

We are pleased to cosponsor the workshop described by Dr. Gordon, which opens tomorrow, on the integration of complementary and alternative therapy in cancer care. We look forward to continued interaction with the complementary and alternative medicine community in our efforts to improve prevention, screening, early diagnosis, treatment, and quality of life for women with cancer. I would be happy to answer any questions you might have.

[The prepared statement of Dr. Trimble follows:]

For Release Upon Delivery

THE ROLE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE IN THE DETECTION AND TREATMENT OF WOMEN'S CANCERS

Edward L. Trimble, M.D., Head
Surgery Section, Division of Cancer Treatment and Diagnosis

National Cancer Institute
National Institutes of Health
Department of Health and Human Services

Hearing before the House Committee on Government Reform
June 10, 1999
2154 Rayburn House Office Building

Good morning. I am Ted Trimble, M.D Head of the Surgery Section, Division of Cancer Treatment and Diagnosis at the National Cancer Institute (NCI). I am pleased to be here today to talk with you about the NCI and the evaluation of complementary and alternative medicine in women's cancers. We at the National Cancer Institute recognize that this is an important and challenging issue, and we have taken steps to significantly alter our approaches to complementary and alternative medicine.

Our Nation is experiencing real progress against cancer. This is evident in our cancer incidence and death rates, which are declining. Between 1990 and 1996, these rates dropped for all cancers combined and for most of the top 10 cancer sites. After increasing 1.2 percent per year from 1973 to 1990, the incidence rates for all cancers combined declined an average of nearly 1 percent per year between 1990 and 1996. The peak year was 1992; from 1992 to 1996 the rate decreased 2.2 percent per year. This confirms the continued downward trend that was reported to the nation in 1998 for the period 1990 to 1995. The rates declined for most age groups, for both men and women. The overall death rate declined an average of 0.6 percent a year from 1990 to 1996, with the declines greater for men than for women.

Advances in Knowledge

While these declines are encouraging we continue to strive to accelerate and extend our progress so that all population groups may benefit. The National Cancer Institute is steadily building an environment that fosters the convergence of ideas from traditional and alternative approaches to the goal of eradicating cancer. The collective oncology research community has made exciting advances in understanding the biology of cancer and developing new ways to screen, diagnose, treat and prevent cancer.

Angiogenesis

Particularly compelling is new information about the development of blood vessels, or angiogenesis, and the cancer cell's ability to exploit this natural process. A number of angiogenesis inhibitors, which arrest tumor expansion by curtailing the formation of new blood vessels and, subsequently, the delivery of oxygen and nutrients to the tumor site, are undergoing testing in clinical trials. One of the agents set to be evaluated this year in a phase III trial co-sponsored by NCI and the National Center for Complementary and Alternative Medicine (NCCAM) is Neovastat, a preparation of shark cartilage. For many years other preparations of shark cartilage have been available as dietary supplements and have been used widely in the United States and abroad for treatment of cancer. Other anti-angiogenic drugs are under investigation for the treatment of breast and ovarian cancers and NCI continues to support a broad range of research projects addressing angiogenesis inhibition in breast and ovarian cancers, among others.

Cancer Genetics

The remarkable gains made in the area of cancer genetics have continued to direct progress in the screening and treatment of cancer and NCI has developed tools to maximize the benefit of this expanding collection of information. The Cancer Genetics Network is a group of family registries for breast and ovarian, as well as prostate cancers, enabling researchers to have access to information about inheritance patterns in these types of cancer. Researchers sponsored by NCI continue to study the tumor suppressor genes, BRCA1 and BRCA2. Mutations in these are sometimes present in inherited cancers, but not generally in spontaneous tumors or normal tissue. NCI has established the Genetic Annotation Index, a catalog of variations in cancer-related genes; and the Cancer Genome Anatomy Project, which has the goal of indexing all expressed genes in a given type of cancerous cell. To date, this database contains over 15,000 DNA sequences for breast cancer alone, of which more than 350 are novel genes. Also listed are around 600 unique genes in ovarian tissue, 3 of which have been linked to ovarian cancer. This type of information can be used to identify possible targets for molecular approaches to the diagnosis and treatment of cancer. In March, the NCI issued an invitation for applications for cooperative agreements to establish a national network that will have the responsibility for the development, evaluation, and validation of biomarkers: cellular, biochemical, molecular, or genetic alterations by which a normal or abnormal biological can be recognized or monitored. The NCI funds resources to make available breast cancer tissue specimens to researchers to study potential molecular markers.

Molecular Markers

Advances in the identification of molecules unique to or overexpressed in cancerous cells have led to sophisticated new treatments for many types of cancers suffered by women. The cell surface molecule, HER2/neu, was originally valued as a prognostic factor for breast cancer. NCI continues to support clinical trials gauging the usefulness of a new drug, Herceptin, a monoclonal antibody targeting HER2/neu for treatment of both breast and ovarian cancer in conjunction with chemotherapy. In addition HER2/neu is under consideration as a target for a cancer vaccine. Selective Estrogen Response Modulators (SERM) modify the effects of estrogen on breast tissue and have been prescribed as an alternative to hormone replacement therapy in women at high risk for breast cancer. The recent NCI-sponsored Breast Cancer Prevention Trial, which addressed the effectiveness of Tamoxifen in preventing breast cancer in high-risk patients, was stopped due to the obvious benefit to women who received the drug. This year the NCI expects to begin a highly anticipated comparison of Tamoxifen and another SERM, Raloxifene, which was approved for treatment of osteoporosis and has been shown preliminarily to reduce the risk of breast cancer.

CA125 is a molecule produced in normal uterine and ovarian tissue and is elevated in ovarian cancer cells. The NCI is sponsoring an important screening study, the Prostate, Lung, Colorectal, and Ovarian Cancer Trial (PLCO), that is, in part, an evaluation of a variety of techniques, including CA125 testing, for uncovering ovarian cancer.

Studies have revealed that approximately 90% of cervical malignancies are linked to infection with Human Papilloma Virus (HPV). NCI has a new study underway in which researchers are looking for ways to manage the mild cervical abnormalities that sometimes

progress to cervical cancer. The project is designed to evaluate the usefulness of testing for certain types of HPV as a means to differentiate between abnormalities and determine which treatment would be most appropriate. Another important study supported by NCI is currently being conducted in Costa Rica where investigators have screened about 10,000 women to obtain data on the incidence and prevalence of HPV infection and co-factors that increase the risk of cervical cancer. NCI is sponsoring a phase II trail to determine whether or not a carotenoid - rich diet can be effective in reversing mild cervical lesions. Changes in HPV status will be concurrently monitored. In addition, scientists at NCI are leading the development and testing of two promising HPV vaccines: one that could prevent new infection with HPV and another that would treat existing HPV. Vaccines against HPV could be instrumental in significantly decreasing cervical cancer incidence.

Tumor vaccines, which may encourage the immune system to recognize cancer cells, may help the body reject tumors and also help prevent cancer from recurring. Vaccine therapy in the treatment of women's cancers is an area of intense research activity. NCI is supporting clinical trials investigating the safety and effectiveness of several different types of vaccine-based approaches for the treatment of breast, ovarian, and endometrial cancers, as well as cervical cancer.

Natural Products Research

Since 1955, the NCI has screened samples of plant, marine and microbial origin for activity against cancer, and several clinically effective anticancer drugs, including vincristine, vinblastine, etoposide, topotecan, adriamycin, actinomycin, bleomycin and paclitaxel (taxol), have emerged from this program. Taxol's antitumor activity was discovered in the 1960s during a largescale plant-screening. Interest in developing the drug increased in 1979 after scientists found that Taxol has a unique mechanism for preventing the growth of cancer cells: it affects the fiber-like cell structures called microtubules, which play an important role in cell division and other important cell functions. Taxol has been proven, through intensive NCI-sponsored testing, to be effective in treating both ovarian and breast cancers and NCI is supporting continuing efforts to apply use of Taxol to other types of cancer including many types of pelvic malignancies. Another promising alternative is docetaxel (Taxotere, Registered Trademark), a compound that resembles Taxol in chemical structure. The drug's manufacturer is conducting independent clinical trials and is cooperating with NCI to test its efficacy in treating a variety of cancers including ovarian and cervical cancers.

Since 1986, the NCI's Developmental Therapeutics Branch has performed collections of plants and marine organisms in over 30 countries located in tropical and subtropical countries worldwide. Over 50,000 plant and over 10,000 marine organism samples have been collected through contracts with botanical and marine biological organizations, working in close collaboration with qualified organizations in the source countries. In addition to testing for activity in the NCI anticancer screens, over 110,000 extracts of these samples are available for testing by investigators at other NIH institutes and in the extramural community for activity against the whole spectrum of human diseases, including cancer, AIDS and opportunistic infections, and diseases of concern to the source countries, such as malaria and other parasitic diseases.

Other Treatment Advances

There has been real progress in successful management of cancers occurring in women. Chemotherapy or hormonal therapy administered prior to surgery has improved overall survival for many breast cancer patients. Women with invasive cervical cancer in five different randomized clinical trials benefited from the use of radiation therapy and chemotherapy given together; until now only one or the other was chosen.

NCI continues to support basic and applied research in many areas. We are moving ahead with a number of research efforts that involve the evaluation of CAM approaches to cancer-related problems. NCI, along with NCCAM, is supporting an evaluation of Dr. Nicholas Gonzalez's nutritional therapy at Columbia Presbyterian Medical Center, one of the NCI-designated Comprehensive Cancer Centers. At present, patients are being screened for the study. Another interesting area of potential research activity is the evaluation of green tea as a cancer prevention strategy.

By employing rigorous methodologies to studies in complementary and alternative medicine, NCI has awarded and continues to support many high quality CAM-related research projects. Among the many research efforts underway are projects examining the effects of dietary interventions in cancer treatment, projects examining the therapeutic value of vitamins and minerals in cancer treatment and prevention, studies in stress and pain management to enhance the quality of life for cancer patients, and studies examining the effect of natural inhibitors of carcinogenesis.

Complementary and Alternative Medicine

The NCI is moving very quickly in important directions to develop CAM information and expand research opportunities for CAM investigators. These activities are broad in scope and include strengthening our relationship with the NCCAM, the careful evaluation of CAM therapies, and the development of accurate CAM information for the public.

Recently, Requests for Applications (RFA) have been issued by NCI in conjunction with NCCAM and other Institutes. The intent is to establish Centers for CAM Research that would provide the resources necessary for the rigorous scientific study of CAM approaches, as well as Specialized Research Centers to investigate the biological effects of botanicals, including those that are available as dietary supplements.

We collaborated with NCCAM on the establishment of a Cancer Advisory Panel (CAP-CAM). The CAP-CAM meets 2 to 3 times a year and draws its 15 members from a broad range of experts from the conventional and CAM cancer research community. This group will review and evaluate summaries of evidence for CAM cancer claims submitted by practitioners, make recommendations on whether and how these evaluations should be followed up, and be available to observe and provide advice about studies supported by the NCCAM and NCI, and about communication of the results of those studies. There already are two submissions from the homeopathy community for review and consideration. Rather than have NCI conduct a best case series review independent of the CAM community, the

CAP-CAM will facilitate the joint review of data using this model. We are enthusiastic that this group can work collaboratively in a new partnership between the conventional and CAM cancer research community.

Imaging Research

Medical imaging has experienced astounding advances in the last twenty-five years. X-ray and other techniques allow for the diagnosis of abnormalities of the bones, organs, and other body structures, often before they have caused irreversible damage. Cancers that were once too small to be detected by physical examination can be pinpointed by imaging and treated before they can spread. The early detection of breast cancer by x-ray mammography is an example of the advances made which saves the lives of many women.

Current imaging techniques include more than just the standard x-ray. X-rays can be collected, recorded and analyzed to produce plain images on film or computed tomography (CT) scans. Radioactive materials called tracers, when introduced into the body, seek out a particular organ or structure (such as a tumor) and can yield an image of the organ or structure when special sensing devices detect the decay of the tracer. The responses of tissue exposed to a changing magnetic field can be recorded as magnetic resonance images (MRI). Ultrasound are sound waves of high frequency which can pass through the body and produce images in real time of rapidly moving or stationary anatomical structures.

As a result of these developments, organs deep within the body can now be biopsied by long, thin needles guided safely to their targets by CT or ultrasound scanning, in many cases eliminating the need for general anesthesia and an open surgical procedure. Adaptations of MRI permit the refined visualization even of the arteries of major organs without the need for painful and potentially hazardous injection of contrast material into these vessels. The biggest impact that imaging research has had on women's health has been through the development of mammography.

Mammography

After skin cancer, breast cancer is the most frequently diagnosed cancer in women in the United States. It is second only to lung cancer in cancer-related deaths. It is projected that approximately 175,000 new cases of breast cancer will be diagnosed in 1999, and about 43,300 women are expected to die from the disease this year.[1] A woman's risk for breast cancer increases with age and continues to increase over her lifetime. It is important to understand that most women who get breast cancer have no known risk factors, such as family history of the disease.

Mammography is an imaging process that uses low-dose x-rays to take a picture of the breast. Regular screening mammograms, though not perfect, are the best method available today to detect breast cancer early. Early detection of the disease may allow more treatment

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[1]"Cancer Facts and Figures - 1999", American Cancer Society.

options. For most women, the National Cancer Institute recommends regular screening mammograms every one or two years starting in their forties.

The National Cancer Institute has developed information for doctors to help women who are between 40 and 50 years old decide when to begin having regular mammograms. There are six risk factors that doctors should be aware of that pose a high enough risk to warrant screening for a woman in her forties: previous breast cancer; specific alteration in a breast cancer susceptibility gene such as BRCA1 and BRCA2; a mother, sister, daughter with breast cancer; atypical hyperplasia (a condition where breast cells are both abnormal in appearance and increased in number) on previous breast biopsy; 75 percent dense tissue on mammogram at age 45-49; or, two or more breast biopsies, even if the results are benign. If none of these risk factors are present, three weaker factors still need to be considered: age of menarche; the number of previous biopsies (either zero or one): and, age at their first live birth (the risk for breast cancer for women with no live births is the same as for women who had a child at ages 25-29).

While mammography has had a major influence on women's health in the past twenty-five years, the NCI continues to work on ways to improve imaging methods for cancer detection and diagnosis.

Improving Imaging Methods for Cancer Detection and Diagnosis

The National Cancer Institute (NCI) funds numerous research projects to improve conventional mammography and develop alternative imaging technologies to detect and characterize tumors. For breast cancer screening, high-quality mammography, an X-ray technique to visualize the internal structure of the breast, is the most effective technology presently available. Efforts to improve conventional mammography center on refinements of the technology and quality assurance in the administration and interpretation of the X-ray films. To advance breast imaging, NCI is funding research to reduce the already low radiation dosage; enhance image quality; and develop and evaluate digital mammography as an improvement over the conventional, film-based technique; develop statistical techniques for computer-assisted interpretation of digitized images; and enable long-distance image transmission technology, or teleradiology, for clinical consultations. NCI also funds research on non-X-ray based technologies such as magnetic resonance imaging (MRI), and breast-specific positron emission tomography (PET) to detect the disease.

Digital Mammography

Digital mammography is a computerized technique that captures the image with electronic sensors rather than film, and displays images using an infinite scale of gray tone. This area of research is of great interest. Mammography X-ray films can contain subtle information not easily discernible to the radiologist. Preliminary data indicate that digital mammograms enhance the quality of the image and even magnify the view of specific areas of the breast. This technology is expected to improve the sensitivity of mammography, especially in radiographically "dense" breast tissue, which renders visualization of cancer problematic, and to decrease the radiation dose per mammogram. Digital mammography also will allow advances to occur in computer-aided diagnosis and teleradiology.

NCI funds many studies of this technology, including those of the National Digital Mammography Development Group. This multidisciplinary academic and industrial group is developing and evaluating digital mammography and related technologies such as image processing for improved lesion visualization, computer-aided diagnosis for enhanced image interpretation, and telemammography (electronic image transmission providing access to specialized clinical experts at remote sites). Currently, this group is testing the potential of digital mammography to serve as the next generation screening technology. NCI has also just released 2 new Program Announcements to alert the investigator community and the small business community to the need for and NCI interest in a concerted effort to overcome the problems of display for digital mammograms.

Novel Non-Ionizing Radiation (Non-X Ray) Imaging

Scientists are exploring novel non-ionizing imaging technologies including MRI, ultrasound, optical imaging, and other technologies. The NCI-funded studies encompass basic technology and instrumentation development through pre-clinical and clinical testing. There are currently 41 NCI-funded projects that aim to define the precise role of these technologies in detecting and characterizing breast tumors.

MRI, Ultrasound and Optical Technologies

Of novel non-ionizing technologies, MRI and ultrasound have been the most studied as ways to improve the sensitivity of breast cancer detection and staging. Both have shown potential for improving differentiation between benign and malignant lesions and in detecting tumors in dense breast tissue. Furthermore, MRI appears unique in its ability to define local anatomic tumor extent, or staging, critical for treatment planning. NCI funds a Cooperative Group of 14 medical centers that is evaluating the use of MRI to improve diagnosis of breast abnormalities. Preliminary results are encouraging, and the Cooperative Group has begun to study the value of MRI in screening for early breast cancer in women at high risk, such as those with a strong family history, or who carry the BRCA1 or BRCA2 genes. The Group is now in the process of expanding the study to include women who received radiation for treatment of Hodgkins disease. Such women are at high risk for developing breast cancer several years after their therapy for Hodgkins disease.

MRI and ultrasound have their limitations, too. One disadvantage of MRI is its requirement for the use of injected contrast material. NCI is funding some projects to study MRI techniques that will enhance the natural tissue contrast between normal and abnormal tissue. Advances in such techniques could lead to cancer detection without injecting contrast material. NCI funds a Cooperative Group of eight centers exploring the value of magnetic resonance spectroscopy (MRS) in four different cancers, one of which is breast cancer. Another property of tissue which physicians have used for centuries is the difference in hardness of normal and cancerous tissue, measured now by palpation. An equivalent method for "palpating" tumors deep in tissue is to measure the tissue elastography (compressibility). This can be done with either MRI or ultrasound, and NCI funds projects evaluating both approaches.

About half of cancers detected by mammography appear as a cluster of microcalcifications. Ultrasound does not consistently detect microcalcifications, nor can it detect very small tumors. Another limitation of ultrasound is that is not an automated, reproducible procedure. NCI is funding two research projects on two different techniques that detect calcifications by ultrasound. Several NCI-funded projects are improving the ability of ultrasound to detect very small cancers, and one project supports the development of an ultrasound device that produces images similar to a computed tomography scan, thus automating the procedure. Progress in all of these areas may come together to make ultrasound an alternative to mammography for breast cancer screening.

Recent technical advances in fiberoptic and laser technologies make optical imaging an exciting new area of potential for early cancer detection. NCI is funding eight projects exploring the use of optical techniques to improve breast cancer detection. Optical signals carry very specific information about the biochemical makeup of the tissue, but localization in space is not as good as with MRI or ultrasound. Therefore, some NCI-funded researchers are developing devices that combine optical techniques with ultrasound, for example, to combine the strengths of both approaches.

Optical technologies also show considerable potential for a variety of other tumors, most notably cancers of the cervix or ovary. Optical detection, diagnosis, and subsequent therapy of early cervical cancer are possible at a single visit, thus eliminating some of the problems associated with PAP smears. Optical technologies applied to the detection of ovarian cancer may bring some progress to this difficult medical problem which has eluded early detection despite advances in so many other areas.

Breast Biopsies

Imaging is also being tested as an aid in performing biopsies. The majority of women in the United States (80 percent) who undergo surgical breast biopsies do not have cancer. As an alternative to surgical tissue removal, image-guided, needle breast biopsy is being studied for women with non-palpable lesions. (Women who have large, palpable lesions usually undergo needle aspirations to determine if their lesions are fluid-filled benign cysts). Image-guided needle biopsy offers the potential advantages of minimized tissue damage, reduced waiting time until diagnosis, and cost savings. A multi-institutional research program is now testing the efficacy and cost-effectiveness of the large-core and fine-needle biopsies compared with more extensive surgical biopsies. (See attached list).

Other Areas of Study

In addition to research on imaging technologies, other research is developing methods to detect products of breast cancer (antigens) in blood, urine, or nipple aspirates, and to detect genetic alterations in women who are at increased risk for breast cancer. Once cancer is diagnosed, studies of these types contribute to characterization of breast tumors and can be useful in treatment planning. Still other NCI-funded projects seek to increase the utilization of mammography among women in age groups for which mammography has proven benefit. An emphasis is increasing utilization among minority and medically underserved women.

Unconventional Innovations Program

In addition to current imaging research being planned the NCI recently created an Unconventional Innovations Programs (UIP) to spur development of daring technologic improvements in cancer treatment and detection in the 21st century. The five year, $48 million program seeks to stimulate development of radically new technologies in cancer care that can transform what is now impossible into the realm of the possible for detecting, diagnosing and intervening in cancer at its earliest stages of development.

Envisioned are futuristic technologies that may sound like Star Wars medicine, but which are grounded in scientists' rapidly evolving grasp of how alterations in the molecules within our cells may lead to cancer. These technologies would enable physicians to scan the human body for molecular changes that foreshadow disease and, once detected, to intervene with minimally invasive procedures, including some that may seem like science fiction - such as injectable miniature robotic devices (nanorobots) capable of killing tumors or "smart" polymers that both detect cancer and deliver drugs.

To aid in identifying technology opportunities that could contribute to the stated goal and fundamentally change the way we detect, diagnose, and treat cancer, the NCI solicited input from the scientific community in the fall of 1998 in the form of white papers. Ideas and information submitted by investigators have contributed to the definition of scope for a Broad Agency Announcement (BAA) solicitation of contracts for the development of "Novel Technologies for Noninvasive Detection Diagnosis and Treatment of Cancer." Proposals were due April 15, 1999, and we are planning to make contract awards by September 1999.

The UIP will take a new management approach to the development of technology that will target quantum improvements in existing technologies or entirely new approaches, rather than incremental improvements to the state of the art. UIP management will actively recruit the interest and involvement of investigators from disciplines that have not traditionally received support from the NCI in taking on the defined technology challenge.

Survivorship

Although cancer remains among the worst fears of Americans, it is becoming increasingly clear that cancer is not the "death sentence" it once was. More than 8 million Americans alive today have a history of cancer. The past ten years have seen an explosion of new and effective treatments for cancer. The emergence of these treatments has enabled some researchers to turn their attention to developing treatments that are well-tolerated and effective, and to interventions that will help ameliorate the worst side effects of the treatment and the disease. Measurement of a patient's quality of life now is included routinely as a component of most NCI-supported clinical trials. Some of NCI's primary quality of life activities and research areas cover several areas.

Supportive Care

The side effects of cancer treatment can not only severely impair a patient's quality of life, but may also leave the patient unable or unwilling to continue with a recommended treatment regimen. NCI continues to pioneer studies on pain relief, fatigue intervention, and the alleviation of other problems that accompany a cancer's progression.

Access to Clinical Trials

NCI believes that clinical trials offer excellent, state-of-the-art treatments for cancer patients and should be accessible to any patient diagnosed with cancer.

Rehabilitation

Even when someone is successfully treated, effects of their disease may remain. Ongoing NCI-supported rehabilitation studies include research on a variety of interventions to aid in more normal functioning.

End of Life

Despite our advances, more than 1,500 Americans die each day from cancer. NCI is actively studying end-of-life issues. In addition to ongoing research in this area, NCI, in conjunction with several offices and other institutes at the NIH, is now currently soliciting proposals for research on ways to ease the final days of cancer patients who can no longer withstand treatment.

Long-Term Survivorship

As more people survive cancer longer, the needs of long-term survivors are gaining increased attention. Because recovering from cancer and living as a cancer survivor are new challenges, the National Cancer Institute (NCI) has established the Office of Cancer Survivorship (OCS) to explore the physical, psychological, and economic well-being of individuals who are cancer survivors. The OCS will support research covering the entire spectrum of issues facing cancer survivors. Areas in which there is opportunity for progress include:

long-term medical and psychosocial effects of cancer treatment;
factors that predispose survivors to second malignancies;
reproductive problems following cancer treatment;
insurance and employment issues unique to cancer survivors.

Information Resources

Communicating with cancer patients, individuals at high risk for cancer, the general public, and the health care community is a central component of NCI's mission and mandate.

Our programs are based upon needs identified through epidemiologic studies and market research among specific population groups, resulting in programs that are relevant and understandable to each group. Our patient education program, leadership initiatives for special populations, and minority research networks are all actively involved in spreading state-of-the-art information about cancer prevention, detection, diagnosis, treatment, and care.

Public Information about CAM

Of considerable importance to all of us is the public availability of accurate, up-to-date information about CAM therapies. NCI has taken steps to assure that this information receives the same consideration as conventional approaches in our evaluation and dissemination efforts.

Detailed CAM summaries are being prepared for cancer therapies identified by our Cancer Information Service and the NCCAM Clearinghouse as being of public interest. The development of these summaries will follow the same model as those for conventional therapies and include specific trial results and references to the published literature. They will be reviewed by the appropriate Physicians Data Query (PDQ) Editorial Board depending on whether the intervention is for the treatment or prevention of cancer or used as a supportive care intervention. In addition, these summaries will be sent to experts in the CAM community for review and comment before they are made available on the NCI web site. Reviews are in progress for shark cartilage and hydrazine sulfate; summaries for laetrile, Essaic, and antineoplastons will be drafted in the near future.

Several months ago, as a result of our own concerns and the constructive input from the CAM community, we removed from the NCI web site all previous CAM information and are creating new information that treats CAM dispassionately and fairly. We are in the process of completely rewriting all the NCI fact sheets that deal with CAM, with hydrazine sulfate and antineoplastons being the first therapies newly available on the web site.

We have established a lecture in CAM at the NCI as part of the medical grand rounds series in our Division of Clinical Sciences and open to all members of the NIH community interested in CAM approaches. The first CAM lecture will be presented by Dr. John Potter on July 20, 1999. The NCI has also initiated a Cancer Complementary and Alternative Medicine Research Interest Group. Dr. Eloy Rodriguez of Cornell University gave the first lecture in this series on April 2, 1999.

The primary avenues NCI uses to communicate with the public and the health care community are:

World Wide Web (http://www.nci.nih.gov): Currently NCI is redesigning its web site to increase its usefulness as a communication tool. The new web site will be organized so that clinicians, researchers, and the public can quickly and easily locate up-to-the-minute information that is relevant to their needs. A new addition to NCI's Web site is the CancerTrials site (http://www.cancertrials.nci.nih.gov). Through this site, patients, health care

professionals, and the public can learn about ongoing NCI-sponsored trials, read about the most recent advances in cancer therapy, and explore other information resources related to cancer treatment. This web site was used by many patients and others who wanted information about treatment advances publicized over the past several months.

Cancer Information Service: The CIS provides accurate, up to date cancer information to patients and their families, the public, and health care professionals in every state through 19 offices located at NCI-funded Cancer Centers and other health care institutions. By dialing 1-800-4-CANCER, callers are automatically connected, free of charge, to the office serving their region. Information on specific cancer types, state-of-the-art care, clinical trials, and resources such as support groups or screening and smoking cessation programs is provided in English or Spanish by specialists who respond to more than 600,000 inquiries annually. The CIS regional offices are NCI's focal point for state and local cancer education efforts that target underserved, high risk, and low literacy populations. Thousands of patients and others called the CIS to get more information about recent treatment advances that were in the news. The system is experiencing a higher busy signal rate that NCI wishes and efforts are being made to address that problem.

Physician Data Query (PDQ): Patients and health care professionals want and need access to accurate, up-to-date, comprehensive information about ongoing clinical trials. Through PDQ, NCI provides information about NCI-sponsored trials. We are in the process of expanding the database, with the cooperation of patient advocates, the Food and Drug Administration, and the pharmaceutical industry, to include all cancer clinical trials approved by the FDA and to revamp the way information is presented. This system has served as a model for other institutes at the National Institutes of Health, and we want to ensure that it continues to be responsive to the needs of the communities we serve.

Medical choices are increasingly made on an individual basis, requiring that physicians and their patients have access to the resources needed to make an informed decision about their treatment and care. Communicating the importance of research findings to physicians and patients in a clear and understandable manner is central to making critical decisions about a patient's treatment and care. NCI is committed to improving public understanding of emerging science and will continue to work with its public and private partners to raise public awareness of key issues in the treatment and prevention of cancer. NCI will work with its partners to provide the public with accurate, useful, and timely information for physicians, cancer patients and their families.

I will be happy to answer any questions.

Mr. BURTON. Thank you, Dr. Trimble. Let me start with you. I am not sure I understood exactly what you just said about the lymph nodes. Is there a non-invasive way to check the lymph nodes? Is that what you are saying? So you don't have to remove them? So that you would not run the risk of lymphedema?

Dr. TRIMBLE. What has been shown in smaller studies is that by the use of either a dye or a radioactive material, one can find the one or two lymph nodes to which the cancer drains. Those lymph nodes are removed and then examined microscopically. If those lymph nodes are not involved by cancer, then that person does not need a full axillary lymph node dissection. So that's the theory that supports our trial, in which half the people would get a full lymph node dissection, and the other——

Mr. BURTON. Let me just ask you, in some cases, they don't take out all the lymph nodes. They just take out some of them. If they take out some of the lymph nodes, don't people run the risk of getting lymphedema, even though they haven't taken them all?

Dr. TRIMBLE. Well, the risk of—you are correct. There is a risk of lymphedema with only removing some. But in, let's say when a full axillary lymphedectomy is performed, then 20 to 30 lymph nodes may be removed. Whereas in the new sentinel lymph node procedure, only one or two lymph nodes are removed. So the incidence of lymphedema following that sentinel node procedure is almost nothing.

Mr. BURTON. I see. OK. So instead of taking out 20 or 25 and then finding 5 that had cancer cells in them, you would just take out those that you were able to pinpoint through the radiation?

Dr. TRIMBLE. Right. Pinpoint that those are the ones that are closest to the cancer. That is where the lymph fluid would drain from that tumor.

Mr. BURTON. I see. OK. All right.

Dr. Beilin, you and I talked before the hearing. We were talking about other forms of cancer, such as prostate cancer. You told me that in Europe, they are using a new technology that would eliminate, in many cases, the need for, let's say, in prostate cancer, the prostate to be removed. You could just attack the cancer and part of the prostate. Is that correct?

Dr. BEILIN. Well, I hesitate to say eliminate the need for it, because every case is individual, and I think that we need a lot more research to be done. But currently there are a number of hyperthermia devices, one in particular is made in Spain, that is going through FDA review right now to be brought over. That involves a penetrating radio frequency hyperthermia that heats tissue beneath the surface of the skin that specifically could be directed toward tumor. There is fair science behind it. So there is a stack of literature that is available privately now, because it's being FDA reviewed by the company. That's just all I know about it.

Mr. BURTON. How long has that been used in Europe?

Dr. BEILIN. It's about 6-year-old technology that's now getting to be big in Europe.

Mr. BURTON. If it's 6 years in Europe, they must have records on this.

Dr. BEILIN. Yes, they do.

Mr. BURTON. Well, does the FDA here in the United States ever solicit those records, or do they just start all over from scratch?

Dr. BEILIN. That is a very interesting question. My impression with working with the FDA that I have done with the regulation thermography is that they look at most cases as new, and that they do not ask for studies that have been done in foreign countries such as Germany, Switzerland, countries that have the integrity of medicine that we do here. There are countries that are developed in the Western world just like ours, and I think that there should be some kind of movement to accept or at least be interested in the review of previous research that's been done abroad with such things as diagnostic early screening equipment.

Mrs. Mack, who spoke earlier, she said she did an early detection by palpation, by just feeling. Well, the tumor, when it is 1 centimeter in diameter is already multi-celled with thousands of cancer cells. That is not really early detection. We are talking about recognizing patterns of disarray and the control of tissue 5 years before it would be visable by other methods. So I think we need a little bit of creative expansion in our paradigm.

Mr. BURTON. Let me ask you about our paradigm. So there are two examples of where the FDA is looking at new technologies that have been used in Europe from anywhere from 6 to 10 years.

Dr. BEILIN. From 6 to 15 years.

Mr. BURTON. From 6 to 15 years.

Now you are here from the FDA, are you not? Do we have anybody here from the FDA today? You are from the FDA? Could you come up to the table, please? Are you prepared to answer any questions? You are only here to monitor the hearing?

Well, I will give you a question. We have been told in the last 24 hours of two cases, one involving the instrument involving hyperthermia, and the other instrument we're talking about as far as early detection is concerned, even before it's readily apparent through mammography or through physical testing, that these have been used in Europe for 15 years in one case, and 6 years in another, and they have not yet been approved by the FDA, and they could be a real adjunct to our therapies and research here in the United States and early detection. I would like for you to have the head of the FDA give me a written reason on why they are dragging their feet on these two things. OK? I would like to have that as quickly as possible.

Dr. BEILIN. Mr. Chairman, if I may add that recently, the FDA has made some changes that are actually positive in that they have granted new areas of possible registration of instruments, diagnostics and treatment that has allowed for marketing approvals more readily than they used to. So at the same time, they may seem slow to acknowledge technologies that have existed with good data, they are also moving in the right direction, from what I can tell.

Mr. BURTON. Well, I'm glad to hear that, but we still have technologies that could really, really help, at least from every appearance that I have seen, that they are still dragging their feet on. I just hate to see any bureaucracy get in the way of progress that is going to help save lives.

Ms. Silver, let me just ask you one question, and I'll yield to my colleague. In your statement, and I am trying to recall exactly how you put it, but you indicated that if there's new treatments or new things that people could take who have an illness that's very severe, they should be able to go ahead and take it even though there hasn't been approval yet if their life is at risk. Did I understand you correctly?

Ms. SILVER. I was referring to the complementary and alternative modalities that we practice in our center. In other words, those have not been proven, by and large. But they have not been disproven. That is to say that no one has suggested or proven that those modalities cause harm or are not efficacious. They have simply not been studied. So for that reason, we ask the question should we withhold those modalities, knowing as we do anecdotally that they can be effective with patients.

Mr. BURTON. And your answer is what?

Ms. SILVER. Our answer is we don't want to withhold those modalities.

Mr. BURTON. And you do go ahead and use them at the current time?

Ms. SILVER. We do use them.

Mr. BURTON. Are you having trouble with the FDA because you do that?

Ms. SILVER. No, no. These are non-invasive, apart from acupuncture, but the other modalities are non-invasive modalities. Many of them are mind body techniques that people can use routinely. So there is no oversight, as it were, because these are not drugs and they are not invasive procedures. But we also don't want to hold out false hope. We don't want to claim that any of these things is effective. We certainly don't claim that we cure cancer. We do say though that we can change the quality of life of a patient with some of these modalities, and our patients agree that their quality of life has been improved.

Mr. BURTON. Do you have some questions?

Ms. CHENOWETH. Mr. Chairman, I just want to thank you so much, for your continuing work in this area and your leadership nationally in this area. It is so very important to us in looking at American health and the role of Government in helping the American people stay healthy and to help them have access to the resources that help them stay ahead of the fight before the disease catches up with them.

I experienced a very difficult passing of my own mother through radical, as a result of radical surgery because of cancer. So I have strong feelings about this, and am very grateful to you, Mr. Chairman, and to your witnesses. I think that we in this committee need to focus, as you are doing, on helping Government get out of the way. You know, first do no harm is not only a good motto for physicians, but also for legislators. I am afraid that some of our policies that we have implemented have caused harm to the individual in not being able to take control of their life. I am concerned that whenever we try to help, we end up interfering and making the lives of our constituents harder. That is simply unacceptable.

Too often, access to public treatments is cutoff because the Federal Government is unsure of its safety. But to people with termi-

nal or potentially terminal illnesses, this seems to be a cruel joke, as it was in the case of my family. I think we need, as you have begun, to seriously question the role of Government in relating to certain institutions that may either help or prevent access to either new treatments or to education and information that will help us prevent disease. So thank you very, very much, Mr. Chairman for this hearing.

I want to ask Dr. Trimble, could you explain to me what circadian rhythms are?

Dr. TRIMBLE. Well, circadian rhythms——

Ms. CHENOWETH. In relation to a patient receiving chemotherapy.

Dr. TRIMBLE. Right. Circadian rhythms refer to any of the natural rhythms, whether that is day and night or the seasons and how they affect a person's physiology and the functions of their body.

In this case, we have some preliminary research suggesting that you could decrease the toxicity of chemotherapy if you gave one of the medicines, doxorubicin, at 6 a.m., and the other one, Cisplatin, at 6 p.m. So in a small study, it seemed as though there was less damage to the nerves and less damage to the bone marrow if you staggered the chemotherapy that way.

The NCI sponsored a large study in which half the women received their chemotherapy at any old time, whenever it was ready, prepared by the pharmacy. The other half got it at 6 a.m., and 6 p.m. Then they looked to see whether there was any difference in the toxicity and damage to nerves or to bone marrow. Unfortunately, in the larger study, there was no difference between the two. But we did think it was an important question and we are continuing to look and see how we can decease the toxicity of our therapies.

Ms. CHENOWETH. You know, Dr. Trimble, American women and probably women in most of the Western countries, subject themselves to some unpleasantries, mammograms, pap smears. We are careful about self-examination for breast cancer. With 14,500 deaths from ovarian cancer though in 1999, I am deeply concerned that there is no early detection program for this type of cancer. Seventy-five percent of ovarian cancers are not detected until the later stages of disease. So I wanted to ask you, what is the National Cancer Institute doing to help women be able to detect ovarian cancer before it reaches the critical stages?

Dr. TRIMBLE. Well this is obviously an extremely important area that we have been working on for some time. We are making a number of efforts to try to improve screening and early detection of ovarian cancer. We are funding a very large trial, the PLCO trial, involving 73,000 women and 73,000 men. The women are being, half of them are being screened with ultrasound and a blood test, CON–25 blood test, for ovarian cancer. So that is a test of the best available technology that we have, versus standard medical care.

We are also trying to develop some new tests. We have announced an initiative called the Early Detection Research Network, which is an opportunity for us to encourage laboratory research and clinical research into coming up with new tests, new screening tests for a variety of cancers. I know for this particular initiative,

there are seven laboratories in the United States which specialize in ovarian cancer that have put together an application just to focus on detecting earlier tests in ovarian cancer.

In addition, the NCI is committed to funding what is called a SPORE or potentially more than one SPORE in ovarian cancer. We have a SPORE, which stands for Special Program of Research Excellence, in breast cancer and colon cancer, prostate cancer. It has been a very successful program. It is designed to bring research from the bench to the bedside. Nine centers have applied for that program. Those applications will be reviewed at the end of this month.

So between these three initiatives, we think we are putting a lot of time and attention and money into trying to find a better screening. But you are absolutely right. We need a better screening.

Ms. CHENOWETH. Thank you, Dr. Trimble. I see that my time is up, but I had some questions for Dr. Beilin. So with the chairman's permission, I would like to submit them in writing.

Mr. BURTON. No, you can ask the questions. If you would just yield to me though, I have a question that I would like to add and then I will let you proceed. Will you yield to me?

Ms. CHENOWETH. We're on.

Mr. BURTON. Dr. Beilin, this device that they have used in Europe for 15 years that you demonstrated with your slides earlier, would it detect something like ovarian cancer?

Dr. BEILIN. In some cases. You know, there's no device that is going to be 100 percent or even maybe 80 percent, but there are cases that have been found when they haven't been found in any other way. We send them in. We refer them to radiology or to ultrasound, and do CA–125, the normal blood tests. So we are able to in a small percentage, reveal more than would have normally in other ways been revealed.

Mr. BURTON. I presume it is the same for prostate cancer or cervical cancer, or any other kind of cancer?

Dr. BEILIN. There are more cases found, but it's not a system that in any way could be used 100 percent of the time. That's just not the way to think about these things.

Mr. BURTON. But it would be a good adjunct?

Dr. BEILIN. It would be a great adjunct, and the cost is very little. The machines are costing less than $15,000, which is about a tenth of any of the other medical scanning or radiological devices.

Mr. BURTON. Dr. Trimble, I don't want to put you on the spot or the people over at NCI on the spot, but I can't understand why at FDA there's new technologies that have been used for 15 years with some modicum of success, a modicum of success in Europe, that have not been approved by FDA that could help you in detecting early cancer in places like my colleague was just talking about, cervical cancer and ovarian cancer. It seems to me that the bureaucracy isn't working together and there's no communication back and forth.

I mean if this has been going on for 15 years, even if it would only help one-tenth of 1 percent of the women who have ovarian cancer, it is something that should be looked at. Does your agency ever talk to FDA or look at these things that are going on in Europe and elsewhere?

Dr. TRIMBLE. Well, we have very close relations with the FDA, particularly in the areas of chemotherapeutic drugs. We have worked closely with them to design really international systems for monitoring toxicity of drugs and response to chemotherapy, in part so that as products are developed in Europe, we might be able to use that data to submit it to the FDA for approval, so we would not have delays waiting for data to come in on patients in the United States.

Mr. BURTON. Have you ever heard of this machine before that's been used in Europe?

Dr. TRIMBLE. I work in the division of cancer treatment, so we have been focused on treatment. We have opened several new initiatives in imaging, one for unconventional imaging. We have also recently funded the American College of Radiology to set up an imaging network to evaluate new imaging in the treatment of cancers. I met yesterday with Dr. Beilin to discuss how this particular technology could be integrated into our research portfolio.

Mr. BURTON. As well as the other technology he was talking about, the heat device? You talked to him about that as well?

Dr. TRIMBLE. No. I did not talk to him about that yesterday, but we would be happy to talk with him.

Mr. BURTON. I wish you would, because it sounds like it's very promising, and it's been used for 6 years in Europe and it's not moving very fast through FDA.

Can I make a request, and if you would write this down I would really appreciate it. I would like to request that the NCI provide a list to our committee of the cancer treatments, including drugs, devices, and other therapies that are available in Europe and Canada that are not available in the United States. The reason I am asking for that is because I have a feeling that you, and I'm sure you are very dedicated scientists as well as your colleague back there, but I have a feeling because there is so much on your plate right now, a lot of these things that are happening in other parts of the world that may have been going on for some time, may not have been really explored. As a result, some of those things, may be a good idea that might help us.

I can remember after World War II, we were bringing all the rocket scientists over here from Germany, many of whom should have been strung up, to help us with our rocket program because they were so far advanced and so far ahead of us. I would just like to know if you could give us a list of all these drugs, devices, and other therapies that are available in Canada and Europe that are not available here, because if we get that list, then we can start seeing what might be helpful. Then we can talk to you about those.

This is not in any way to denigrate the work you are doing. It is just to say that there might be some adjuncts out there that could be helpful to you.

Dr. BEILIN. Mr. Chairman, if I might ask the question of Dr. Trimble.

Mr. BURTON. Sure.

Dr. BEILIN. What is the status of mistletoe, because mistletoe therapy is being used in many oncology clinics in Europe? From what I understand, is that our drug companies here are trying to recreate a patentable mistletoe to be used as chemotherapy, but

without the original mistletoe therapy with the research results that they have gotten being acceptable by FDA.

Mr. BURTON. Before you answer that question, Dr. Trimble, this is one of the things that really bothers a number of people in Congress, because many people in Congress, including myself, suspect that some of the pharmaceutical companies have undue influence at the Food and Drug Administration and some of our National Health Institutions. I hope that's not the case, but we have that concern. When we hear things like what he just mentioned, that there is a therapy or a substance that is being used like mistletoe in Europe to help in areas like chemotherapy, and instead of using that or exploring what Europeans have done, which is very cost-effective and inexpensive, we have got the pharmaceutical companies trying to come up with something that is patentable from some synthetic property, some synthetic thing. The FDA then tests it, runs it through, they get a 6, 7, 8, or 9 year patent—I don't know how long the patents run on those things—so that they can make money. Who suffers? The patients do when there might be something much less expensive that's on the market over in Europe. Those are things that really bother people in this country.

Anyway, go ahead. I'll let you answer.

Dr. TRIMBLE. Well first, I'll take a pass on the mistletoe because I do not know anything about it. We will get back to you. But that is not an area that I have studied.

Mr. BURTON. OK. Well that would fall under the category of all the questions I just asked.

Dr. TRIMBLE. Yes. No, I can comment or I would like to comment on our interaction with our colleagues in Europe and elsewhere. The National Cancer Institute has made a sincere effort to exchange information with colleagues from around the world. We sponsor a meeting in conjunction with the European Organization for Research and Treatment of Cancer every 2 years, to discuss new drug development. We have regular meetings with colleagues in Japan. We also have been strengthening the ties between our clinical researchers in this country, those in Canada, and those in Europe.

Approximately 3 weeks ago, at the national meeting of the American Society for Clinical Oncology in Atlanta, I participated in a meeting to discuss trials in ovarian, cervical, and uterine cancers with representatives from Australia, Scotland, England, Norway, Sweden, Germany, Austria, and Italy. This is something that is happening in many other cancer sites as well. So we are definitely trying to find out what is going on elsewhere around the world, and make sure that people in the United States have access to the best ideas, wherever they are from.

Mr. BURTON. Dr. White, I understand that you may know something about the question that was asked about mistletoe?

Dr. WHITE. Yes. I can tell you a little bit about what we have done in this area. As you probably know, the National Center for Complementary and Alternative Medicine has 10 or I guess now 13 centers that it funds for various different diseases. It has a cancer center at the University of Texas, Houston, which we, NCI, co-funds with the NCCAM. That center is actually doing a phase I study of mistletoe in advanced esophageal cancer. They also have

done a variety of pre-clinical studies with other herbal approaches that are used outside the United States predominantly.

There are a variety of different preparations of mistletoe that are used in Europe and in Australia and various places. This is using one of those five or six that are available.

Mr. BURTON. How long has it been used in Europe, do you know?

Dr. WHITE. I don't know when it first started. The last randomized clinical trial that I am aware of that was done in Europe was published in 1988.

Mr. BURTON. 1988?

Dr. WHITE. Yes.

Mr. BURTON. That was 11 years ago. And we haven't gone through the studies yet on it here in the United States?

Dr. WHITE. Well, there has not been a study done in the United States, that I am aware of. But the review of that material, as I said, has been done at the University of Texas.

Mr. BURTON. You know, I have had cancer in my family. I have had people appear at this table here who have little children who are dying, and there's alternative therapies available to them, and we run into stonewalls with some of the agencies, FDA or others, and even doctors who have used some of these therapies they have tried to put out of business. When we hear of therapies, technologies, or simple products like mistletoe, that's being used in Europe with some effectiveness, and people are dying here, and I have to look at these kids and their parents, or some men that had Hodgkins disease that was going to be terminally ill, and he had to go outside the bounds of what's considered law and order to be treated, it really boggles your mind and bothers you. I just can't understand why we are having this kind of a problem.

If there is a technology or some substance that can be used in Europe and is being used for 10, and you said 11 years ago they were testing this and using it, why is it that the United States, the most advanced country in the history of civilization, is 11 years behind, 15 years behind in this other area, 6 years behind in another area, and when I ask these questions, they say of the FDA, this young lady that's sitting back there, she says, "Well we'll check on it and get back to you." But there really isn't any answer. I just don't understand it.

It seems to me that Dr. Trimble and you, Dr. White, and others, ought to be constantly looking at these alternative therapies along with the Food and Drug Administration, to try to make sure that we are giving the American consumer, the American patient, the very best opportunity to live a healthy life and to survive if they are in big trouble. I know you are trying to do that. But it seems to me that some place the golf club is missing the ball. That is why I asked that question of Dr. Trimble, that we get a list of all the cancer treatments they are using in Canada and Europe, and the devices and the other therapies, so that we can at least look at them and see what the heck is going on over there that we are not doing.

It is really frustrating to me when I hear this kind of stuff. Go ahead.

Dr. WHITE. Yes. I would just like to put a little bit of perspective on the mistletoe issue. I understand the broader scope of what it

is that you are saying, but specifically on mistletoe, the largest clinical trial that I am aware of was a randomized trial with three arms on it, one arm that patients did not receive any supplemental care after their surgery—this is for breast cancer. Another arm received standard chemotherapy, plus or minus radiation therapy for their breast cancer. This is all adjuvant therapy. The third arm received mistletoe.

The mistletoe arm did better than no therapy, but the chemotherapy arm did better than no therapy. The mistletoe arm did no better than chemotherapy. So I think it's not—so we're talking about first of all, adjuvant therapy. So this is not in advanced forms of cancer. Second, it is not something that represented in that study a step above what was already available to the patients.

Mr. BURTON. Dr. Beilin.

Dr. BEILIN. If I may comment that there are statistics being gathered an immunologist and oncologist colleague in Austria for the Germanic countries. They have discovered that statistics seem to be coming out that using chemo plus complementary therapy such as mistletoe together resulting, like in breast cancer, the number is 25 percent less recurrence rates when you use both together. So I think that those kind of statistics need to kind of leap over here so that we can begin to take the best and to integrate them and add them together to have an additive effect. That same statistic came out for prostate and melanoma.

Dr. WHITE. Is that published information?

Dr. BEILIN. I believe so. I can lead you to it.

Dr. WHITE. I would be happy to review that.

Mr. BURTON. Well see, this is the kind of communication that every American would like to see all the time, not just at the table here at a hearing.

So let me just ask two more questions, then I'll yield to my colleague. Then we'll wrap this up, because we have all been here a long, long time. The NCI gets $2.7 billion, $2.7 billion for cancer research. You are spending less than 1 percent of that on alternative therapies. We are hearing things here today that indicate that there are some alternative therapies with promise. I am sure you are going to give me a list of other things that have promise that we're going to get from Europe. Why is it that we only spend $20 million out of $2.7 billion on alternative therapies when half of the Americans who have problems are using and trying to find alternative therapies. It just doesn't make any sense to me. Can you give me an answer to that, Dr. Trimble? Why are we only spending $20 million?

Dr. TRIMBLE. Well, as I know that Mr. Chairman, that you have had some discussions with my director, Dr. Klausner, on this issue. We realize that we need to provide the American public with accurate information on complementary and alternative medicine, and we need to provide them with accurate appraisal of these techniques in terms of whether they work so that people in the United States can decide for themselves whether they wish to avail themselves of various complementary and alternative medicine techniques.

Mr. BURTON. But I think you are making my point. We need to spend more money than just less than 1 percent on that. Wouldn't you agree with that?

Dr. TRIMBLE. Well, I agree that we need to do more research. To that end, we have agreed to co-fund with the other institutes, centers for alternative medicine research across the United States. We are actively soliciting new ideas that we can test at these centers and through with their existing cancer centers. So we hope that we can make more information available and have more and better treatment which combine standard treatment, complementary medicine and alternative medicine for the people of the United States.

Mr. BURTON. Let me yield to my colleague. She has to leave.

Ms. CHENOWETH. Dr. Trimble, could you commit to us how much the National Cancer Institute will dedicate to alternative medicine studies and research?

Dr. TRIMBLE. No. That's above my pay level to make that kind of a commitment. I will commit that we are actively recruiting studies. We have committed to setting up centers to study complementary and alternative medicine. We will continue to forge a joint approach with our colleagues in other medical disciplines in this area.

Ms. CHENOWETH. Mr. Chairman, I wonder as a member of your committee, if I might ask that you would ask whoever is in the pay grade——

Mr. BURTON. Dr. Klausner.

Ms. CHENOWETH. Dr. Klausner, how much? I would like to know as a Congressman.

Mr. BURTON. I think what we ought to do is as the Congress take a look at the amount of money we are appropriating for NCI, and talk to the people on the Appropriations Committee. Maybe since NCI of their own volition isn't going to authorize more money for alternative therapies, maybe we should just specify in the appropriations bill how much you have to spend for that. If we did that, maybe that would break the log jam. But I will try to talk to Dr. Klausner. I want you to make a note that we do that.

I don't have any other questions. Do you have any other questions?

Ms. CHENOWETH. Mr. Chairman, I just wanted to share on the record with you an observation that I have made. You know, we broke all the barriers down when we passed NAFTA and GATT. Now we have the World Trade Organization. We are importing 22 percent of our beef that comes from foreign countries, and we don't know where. They have certainly different standards than we have. Yet we are consuming that beef not knowing that it's coming from foreign countries. Forty percent of our lamb sometimes comes from 7,000 miles away and we don't seem to ask a question about that. You know, we have toys that come from China, and we have hotwheels that come from Malaysia, and we have dog bones that come from Argentina. Nobody seems to worry about that in this whole global economy.

But what about getting information from Europe that we can use on a par the studies and benefit from them? It just seems absolutely incredible to me that we always have to reinvent the wheel when it comes to medicine. Yet in every other arena in this global

economy, but medicine, and freedom from medicine, and freedom from the institutions of the individuals sometimes when we make that choice, is what is sorely lacking.

I am afraid this Congress unfortunately is supporting the institutions and the patients have become a byproduct or just a necessary function for the institutions, instead of the institutions being a necessary function to better healthcare.

So, Mr. Chairman, I would love to work with you on perhaps requiring something in NAFTA or GATT that would mandate that these studies be accepted by FDA on a par.

Mr. BURTON. We'll take a look at it. I will get together with you and we will have Beth look into it, and see if we can't maybe do some of that.

Ms. CHENOWETH. Thank you.

Mr. BURTON. I think that at the very least, those technologies should not languish for 6, 7, 8, 10, 15 years before they are utilized here in the United States.

I was just informed that shark cartilage, for instance, I think Dr. Trimble said they are testing that, 7 years ago they started talking about it and we are just now doing it. So it seems like there is a lot of foot dragging.

Well, I don't have any other questions for you. Thank you, Mr. White. You weren't scheduled to speak, but we do appreciate your coming before us. Dr. Trimble, Dr. Beilin, thank you very much. Ms. Silver, thank you very much. I want to thank you once again for your patience.

We stand adjourned.

[Whereupon, at 3:45 p.m., the committee was adjourned.]

[Additional information submitted for the hearing record follows:]