PNL-9187

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REPOSITORY PNL

COLLECTION Intraesophageal

BOX No. 2947

FOLDER HSC 73-5

W J Bair

DATE 8-28-73 TIME 11:00 A.

WHILE YOU WERE OUT

M Kenneth Swinth

OF 213 272-6511

PHONE UCLA

- [x] TELEPHONED
- [x] PLEASE PHONE
- [ ] CALLED TO SEE YOU
- [ ] WILL CALL AGAIN
- [ ] WANTS TO SEE YOU
- [ ] RUSH
- [ ] RETURNED YOUR CALL
- [ ] YOUR WORK IS READY

MESSAGE I talked with the operator + therefore did not ask what he wanted —

688-2000

FTS 213-~~824-7991~~

54-3000-034 (1-67) AEC-RL RICHLAND, WASH.

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Battelle
Pacific Northwest Laboratories
Battelle Boulevard
Richland, Washington 99352
Telephone (509)
Telex 36921

November 7, 1973

Dear Bill,

I am still somewhat perturbed about the actions of the review committee. I consider the basic project so relatively innocuous (as do many others) that I feel we must not be communicating on all the aspects. I am not aware of the specific objections so I am left in a quandry and can not take any positive action.

I would assume that the objections are in the area of benefit vs. risk. Basically, the probe falls in the same category as any other technique for assessing dose to the inidvidual such as urinalysis, whole body counting, dosimeters, etc. The purpose of these devices is to control the radiation induced risk to the individual and to society and to constitute a legal record of individual exposure. This legal record could be used to limit future radiation exposure or to determine damages for just compensation of the individual. Each of these processes involve risks pecular to the technique and common risks. A common risk which I believe is often ignored is the psychological and possible monetary risks of obtaining a real or false unusually high reading. I would submit that the stress involved for an individual past child bearing age may easily outweigh any somatic risks. Any individual benefit from these techniques is small until the time that overexposure can be medically compensated for in the few cases involving legal compensation.

Basically, the probe adds a new refinement to our measurement techniques and promises the reduction of detection limits. It will refine the measurements of an individual's dose committment and improve our judgement in two areas: 1) Legal compensation, and 2) Decisions to control an individual's working environment. In the sense that such decisions will affect an individual's psychological, family, and financial welfare they are important to him.

I am afraid that many people equate the risk from the probe with the assumed unpleasantness of swallowing it. When the BEIR report came out I made a comparison of risks from gastroscopy and an upper G.I. examination and found them to be roughfully the same. I intend to refine the comparison, but the important point is that one has a rough point of comparison for risks. When judging the risk estimates from gastroscopy one must remember that the medical data used in these estimates involve people with some G.I. abnormality - real or assumed.. Note also that the results of "accidents" in a G.I. exam (G.I. cancer ≃ death) and gastroscopy (perforation ≃ hospitalization) are quite different.

Although there are many aspects of the esophageal probe which could be researched on a continuing basis, the money and time are not

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available to do so. I believe that the present review committee's decisions and the performance on the initial subjects are important determinants in the probe's future. I believe the concept has merit or I would not pursue it.

Sincerely yours,

Ken

Ken

KLS/js

cc:
I.C. Nelson
A.J. Haverfield

Bill,

I have enclosed a slightly updated version of the submittal I alluded to at the Health Physics meeting. I think most of the information has been transmitted to the committee by letter, but I thought you should see it in "one piece." I am still looking for information on anesthesia risks and complications and trying to better define the procedure - both primarily for my own information.

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HUMAN TESTING OF INTRAESOPHAGEAL RADIATION DETECTOR

K. L. Swinth

INTRODUCTION

The purpose of this proposed effort is to evaluate the use of the intraesophageal radiation detector on human candidates. This probe was developed specifically for counting plutonium deposited in tracheobronchial lymph nodes of humans who have accidentally acquired a deep lung deposition of plutonium. Previous publications[1] describe the effort in more detail and also describe the results of some experiments performed on dogs. These experiments demonstrated the usefulness and practicality of an earlier probe. The probe described herein has also been tested on dogs and has easily provided positive counts on a dog with an initial alveolar deposition of 44nCi.

The human evaluation will necessarily be a joint effort. Medical personnel at a recognized center with potential volunteer subjects will be requested to collaborate on the experiment and handle all medical aspects (see below). I will limit my activities to operation of the equipment and data handling.

The discussion of medical procedures discussed herein is not meant to constitute a recommended medical procedure, but is used for planning purposes. The attending physician must decide on medical protocol and watch for the welfare of the subject.

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DESCRIPTION OF PROBE

Coupling a scintillation crystal to a photomultiplier with fiber optics causes an 80-90% loss in the scintillation intensity reaching the photomultiplier. At low energies this is serious because it causes a loss of resolution and moves the scintillation spectra into the noise region of the phototube. For low background counting and an improved signal to noise ratio, one must reduce the background from the photomultiplier. This was done by selecting a low-noise high-gain phototube, magnetically limiting the active area of the photocathode and by reducing the number of fast rise time pulses by a pulse-shape discrimination technique[4]. Use of these techniques reduces the background count rate in the energy range from 6.5-40 keV by a factor of 50 or more.

The NaI(Tl) crystal, surrounded by MgO is encased in a thin aluminum shell (0.25 mm) with a glass optical window sealed in place by epoxy. The detector is coupled to the fiber optic light guide by an optically transparent epoxy, an aluminum ferrule for mechnaical strength and an optically opaque epoxy which also occludes light and fills the remaining void.

The fiber optic light guide is constructed of a 4.7 mm diameter bundle of 50 micron glass fibers having a numerical aperture of 0.66. The ends of the bundles are secured, bonded and polished in stainless steel ferrules to which an opaque outer sheath of polyvinyl chloride is attached.

The completed assembly is coated with a pure polyurethane resin and cured slowly at room temperature and high humidity. This material protects the probe from the caustic fluids within the digestive tract and softens the edges and corners of the probe. Due primarily to the thermal

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sensitivity of the NaI(Tl) crystal the probe can not be autoclaved; however, gas sterilization has been used without degrading the performance or longevity of the probe.

Figure 1 shows a photograph of the assembled probe with the detector and photomultiplier; a preamplifier is encased in the housing with the phototube. This unit uses a 2.5 cm long by 4.7 mm diameter crystal coupled to the photomultiplier by 60cm of fiber optics. Three other probes using a 90 cm fiber optic coupling have been built and resulted in performance comparable to the present unit. Probes could be built in a large variety of sizes and shapes constrained primarily by light collection in the crystal geometry selected and by light transmission of the fiber optics. In general, suitable operation of larger volume detectors (NaI(Tl)) operating at low energies (10-40 keV) would be difficult whereas smaller volume detectors could be easily engineered as could probes for higher energies.

GENERAL SIGNIFICANCE OF PROBE

The intraesophageal probe is important in health protection work for two basic reasons. First, unless the lungs and lymph nodes are treated as a single critical organ it is impossible to interpret the long term significance of count rates over the chest of an exposed worker. Autopsy cases have shown extremely high plutonium concentrations in the respiratory lymph nodes and it is known that a large percentage of the inhaled plutonium may translocate to these nodes over a period of time. Some of my collegues have noted that measurable lung burdens have "disappeared" after a period of a few years. Is this material in the lymph nodes?

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The relative radiosensitivity of the lymph nodes and lung tissue must be resolved by animal experiments. If the lymph nodes turn out to be relatively radioresistant, it may be desirable to develop therapies that will stimulate the transport of deposited material to the lymph system. Presently, the only way the relative concentrations of a material could be determined would be through knowledge of the exposure aerosol and by use of a mathematical model to estimate the translocation to the respiratory lymph nodes. Such a procedure is highly questionable at best. The important point is that we now have a measurable system that can be used to determine the relative partition of material. The ability to measure a parameter in reaserch generally accelerates developments in related areas and allows investigators to look at and answer questions related to the capability (i.e. lymph node role in relation to respiratory depositions).

Aside from the simple partitioning problem, it is important to note that present lung counting techniques are only sensitive to 1/3 to 2/3 of a MPLB* (16nCi). If the MPLB is reduced to 2 to 4nCi as has been suggested, the lung counting capability disappears. With further development and proper use, the intraesophageal probe should be capable of measurements below 1nCi in humans. This would yield a capability of determining low levels (< 5nCi) of inhaled plutonium a few years post exposure, assuming about ¼th of the material is translocated to the tracheobronchial lymph nodes.

If we take the 95th percentile of the high potential cases from LA - 4875, we find about 4.5nCi of plutonium in both the lungs and the lymph nodes. In the method used for sample preparation, these are

* Maximum Permissible Lung Burden

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most likely the same lymph nodes we count, and this is an amount that we can detect. The median for high-potential cases is less favorable with about 0.045nCi in the lungs and 0.003nCi in the lymph nodes; however, it must be noted that some of the exposures are likely due to "injection" rather than inhalation.

Extrapolation to lung burdens is dependent upon an improved understanding of the dynamics of the human respiratory lymph system which is much more complex than that of animals. This problem is being approached under a separate program.

To summarize, the value of the probe is in the following areas of which only items 2 and 3 are of importance for the present discussion.

1. Determining partitioning of material between lymph nodes and lungs in experimental animals. The preliminary work has already been accomplished in this regard.
2. Determining partitioning of material in humans.
3. As a primary method of determining inhaled material at low levels.
4. As a prototype for medical probes that could be used in a number of areas including:
   a. Nuclide uptake for localizing lung cancer during bronchoscopy.
   b. Pulmonary function studies using radionuclides.
   c. Diagnosis of gastric and esophageal lesions by nuclide uptake
   d. Diagnosis of uterine, prostate, and colon lesions.

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BENEFIT TO SUBJECT AND MANKIND

If we demonstrate that the activity is moving to the lymph nodes, we can state (assuming radiation damage to the lung including cancer is dose dependent) that the risk to the lung is decreasing. Thus the subject can be assured that the danger to his life sustaining lungs is decreasing. Although the risk to the lymph nodes would be increasing the lymph tissue seems to be relatively radioresistant. At any rate lymph nodes and associated tissue can be excised without the serious implications of lung removal.

Another potential benefit to the subject would arise in the case of lymph related disease (cancer). Demonstration of a significant deposition of activity in the lymph nodes (potential cause and effect) could help in receiving a favorable legal settlement in court thus providing monetary aid for the subject and his family. Hopefully such a circumstance will not arise, but one cannot deny that a favorable settlement would be of benefit to the subject.

If present research on therapeutic removal of deposited plutonium advances favorably, it will be necessary to know the site of deposition of the material since it is unlikely that removal therapies will have equal efficiencies for different body compartments. Knowledge of the deposition amount and site could be important in the subject's decision to undergo therapy and in the choice of technique.

The value to mankind is a little more general than that to a contaminated subject. Besides offering additional protection to each individual as a potential contaminated subject, the probe demonstrates increasing capability to deal with a potential hazard of the nuclear age.

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Although I could go on about real and possible benefits to the subject and mankind I think I have covered the major points. The possible confirmation of decreasing dose to the lungs, the demonstration of significant lymph tissue doses in legal actions and the knowledge of plutonium partitioning for therapy decisions are all of benefit to the subject.

TENTATIVE PROTOCOL

Outlined below is the present experimental protocol. Medical aspects must be the decision of the attending physician; however, the expected procedure is outlined.

1) At least one hour prior to the measurement the probe and associated electronics will be turned on and tested to ascertain that the equipment is operating properly. This consists of checking electronic settings and counting a standard source in a fixed geometry. A series of room backgrounds will then be taken until the measurement begins.

2) During the equipment preparation the physician will interview the subject making sure he understands the procedure and to determine any possible contraindications. An acceptable informed consent form will be required before the experiment proceeds. (In all probability this portion of the procedure will have been completed in the past).

3) Next, the subject will be administered a local anesthetic if deemed proper by the physician and requested by the subject. Either a flavored viscous jell containing xylocaine and made for this purpose or a topical anesthetic spray could be used.

4) After the anesthetic (if used) has taken effect the probe will be lightly lubricated with a hospital lubricant and inserted down the

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esophagus 27 cm as referenced to the incisors.

5) In order to verify the position of the probe an X radiograph will be taken of the area of interest. If not in correct position adequate corrections will be possible without a second X ray. The detector will be in the correct position when its distal end is about 1 cm below the common segment of the major bronchii.

6) Next, the subject will be placed in a comfortable position and two 10 min. recordings of the count rate will be made. (At LASL the initial positioning and x ray will be done in the hospital after which the subject will be moved to the adjacent building where the whole body counter is located. As I understand it the subject would be transported between locations in a wheel chair. Whether or not the probe is in location during transport will depend on his tolerance of the insertion procedure. Reinsertion to the proper depth will not be difficult.) The probe will then be inserted an additional 4 cm for a 10 min. count and then withdrawn 8 cm for a final 10 min. count.

7) Following completion of the counts the probe will be withdrawn and the subject will be examined by the physician. The physician will also communicate any preliminary findings to the subject if available.

8) Additional room backgrounds and a count of the calibration source will be made following the measurement.

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DISCUSSION OF RISKS

Any activity that one undertakes involves some measurable risk to the individual's well being. These risks are hard to put into perspective and most individuals subject themselves to significant risks (driving, climbing ladders, smoking, etc.) without a second thought. Most medical procedures involve some risk and the individual should not be subjected to these risks without being informed. This section discusses some of the risks involved.

Inherent Risk in Esophagoscopy

I have searched the literature for various risks inherent in esophagoscopy. Since esophagoscopy often involves a gastric examination the risks of esophagoscopy and gastroscopy are often not separated.

Gastroscopy is an old procedure dating back to the 1920's. Initially, a rigid metal tube was used and this involved some definite risks. Three types of severe lesions were observed: 1. Lesion of the hypopharynx, 2. Rupture and perforation of the thoracic esophagus and rupture and perforation of the stomach. In our case we do not have to worry about lesions 2 and 3 since we will not enter the stomach and ruptures of the esophagus usually occured in the last 2-3 cm where it curves before entering the stomach. The most common site of perforation with the solid gastroscope was the pharyngoesophageal region with an overall accident rate of 0.079% and a fatality rate of 0.014% (C. H. Brown ed. Diagnostic Procedures in Gastroenterology). It must be emphasized that these accident rates are before the introduction of the flexible gastroscope and the foregoing is primarily historical information. Any accidents are rare with the flexible gastroscope (R. H. Nelson Gastroscopic Photography) which is similar to the probe we are working

with. In fact, one expert states, "In 1,300 examinations with the rigid gastroscope and in 6,000 with the flexible gastroscope, I have not seen this lesion (lesion of hypopharynx) even once..." (R. Schindler, Gastroscopy). The likely lesion of the hypopharynx is crushing the tissue between a rigid probe and the spinal column.

In recent literature some information on the flexible fiber optics scopes can be obtained. In one compilation of 75,618 examinations the rate of perforation of the pharynx or esophagus was 0.048% (Morrissey, et.al. in Progress in Gastroscopy, 53, p 456 (1967)). In this report, one institution with only 500 cases accounted for about ½ the total accidents. In the same article 829,700 examinations with a gastrocamera (intragastric camera) were noted to have an overall accident rate of 0.0012%. The fatality rate was not noted; however, with modern antibiotics and proper diagnosis this should be small. Another article covering 2052 examinations of the esophagus and stomach with fiberscopes (Lucchini, et.al. Gastrointestinal Endoscopy, 16 p56 (1969)) noted that there were no complications in 349 examinations of the esophagus in unselected subjects. An additional 52 exams were not completed because of lack of cooperation (7), stenosis of esophagus (33), liquid retention (1), and because the probe could not be moved past the pharynx (11).

It seems that with due care and gentleness on the part of the physician complications can be expected to be rare.

I believe we have a moral duty to appraise the subject of the relative risks involved; however, it is not clear this is our legal duty. Apparently the point of "relaively high risk" for collateral hazards is around 1% and is a point at which the individual must be

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made well aware of the collateral hazards. (M. L. Plante, "An Analysis of 'Informed Consent'" Fordham Law Review, 36 p 656).

Anesthesia

Anesthesia always involves some risk from a drug reaction or overdosage. The decision to take this risk must be borne by the physician and subject. Conversations with various endoscopists have been mixed on the need for anesthesia. Recommendations for tranquilizers, local anesthesia and no anesthesia have been received. Some small amount of topical anesthesia may be of significant aid for comfort of the subject.

Asepsis and Material Compatibility

The probe will be cleaned with alcohol and sterile water before use and handled in a "clean" manner. The esophagus is a "dirty" area of the body and normally receives and handles material of doubtful cleanliness (food). It was because of this small risk of infection that the esophagus was chosen as a route of entry rather than the trachea. The detector could be gas sterilized; however, alcohol cleaning and clean handling should be adequate. This is the method of handling common fiberscopes.

Reactions to the material in the probe must be considered. The materials that will contact the esophagus are polyvinyl chloride and the polyurethane covering the detector. The Toxic Substances Handbook (1972 edition) did not list these materials as toxic unless they are thermally decomposed (burned) and inhaled. All elastomers and plastics are toxic if burned. (Bovee and Schubert, Industrial Hygiene Association Journal p 168 (March-April, 1963)).

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X-Radiation

To ascertain the location of the detector it will be necessary to take a radiograph. There is some inherent risk from the x-radiation; however, this can be reduced by two methods; 1. Make the x-ray part of a medical examination or 2. Collimate the beam, use gonad shields, use high speed film, and use high energy radiation. The x-ray will probably have to rely on techniques presently in use at the facility. Experimentation to reduce the dose could result in higher dose due to unsatisfactory initial results.

Other techniques could be developed (ultrasoncis, tactile or auditory location of left bronchus, etc.); however, this would be difficult and would probably involve eventual comparison with x-rays.

Technical Procedures

The probe itself does not offer any apparent dangers other than physical abuse of the subject (i.e. hitting the subject with the probe). The probe is completely passive and the photomultiplier housing which may come within a few inches of the subject is at ground potential. There is no reason for the subject to have contact wiyh the counting electronics, and no potential hazard is anticipated from accidental contact.

Handling of Data

On these initial experiments data will be reported as the number of counts above the supposed background. A calibration will not be attached to the counts because of the relatively large uncertainty in the calibration. Data will be reported as simply negative or positive.

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Medical Responsibility

Presently it is anticipated that the LASL industrial physicians will handly the medical use of the probe. Initial contacts with Dr. George Voelz (M.D.) were favorable and they are in the process of finding employees suitable for testing the probe by looking at technical and phychological factors plus the subject's anticipated willingness. Dr. Whipple (LASL) called me on June 5, 1973 to inform me that LASL's Human Subjects Committee was meeting to review the proposed project and he assured me that I would receive a copy of their conclusions and their informed consent form. When I receive this data it will be forwarded to Battelle's committee immediately. Initially we do not expect to perform this measurement on more than three subjects and this is all that we are requesting initial permission for.

Further interactions (laboratories) and an increase in the number of subjects will be put before the Battelle committee separate from this submission.

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