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Battelle
Pacific Northwest Laboratories

702831

Internal Distribution
W. R. Wiley
W. J. Bair
H. Drucker

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To H. M. Parker
Chairman Human Subjects Committee

From F. P. Hungate FPH

Subject Potential uses of Vitreous Carbon-^{170}Tm Irradiators

We have developed and patented a blood irradiator potentially useful for a variety of clinical applications such as: suppression of early organ or tissue graft rejection, treatment of leukemia, treatment of arthritis and other applications involving cellular immune reactions. We believe the human subjects committee should review the problem prior to the time when pressures develop for clinical testing. The following is provided to assist in such review. If desirable further material can be supplied or a group discussion arranged.

FPH/mlr

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Extracorporeal irradiation of blood has shown promise in suppressing early rejection of renal allografts and in treating chronic lymphocytic leukemia. Previously, nearly all blood irradiation has involved brief intermittent exposures with high dose rates. The small amount of data available involving continuous irradiation of blood suggests that doses given chronically at lower rates are more effective in suppressing graft rejection. However, no suitably portable device has been available to permit evaluation of effects from chronic irradiation. This work has been directed toward developing a fully portable blood irradiator. After preliminary testing of a variety of source materials, ^{170}Tm was selected for its favorable beta energy, low cost, and compatibility with the fabrication requirements. The body of the irradiator is cast from polyfurfuryl alcohol with subsequent high-temperature conversion to vitreous carbon. By sequential layering of the alcohol and suspending of $^{169}Tm_2O_3$ in the midlayer, a unit is produced without any radiation exposure and with the source material contained on both a macro and micro scale. Exposure of the unit to reactor neutrons produces ^{170}Tm without activation of the vitreous carbon. Effects of chronic extracorporeal irradiation of blood are now being studied in large animals.

Tests with goats typically show a drop in circulating lymphocytes to 20% of normal within a week following initiation of treatment with subsequent levels of 10-20% while treatment continues. Following cessation of irradiation circulating lymphocytes gradually rise approaching normal after several months. To date treatments have extended over periods no longer than three weeks because of shunt failure, i.e. clotting in the shunt hardware. Daily doses to blood are calculated to be 1,000-3,000 rads although this can be easily adjusted either up or down by using units loaded with more or less thulium or activated for longer or shorter periods.

Evaluation of skin graft rejection has been only partially successful due to erraticresponses and to failures in maintaining the patency of the shunts following placing the grafts. There is some evidence that rejection is delayed following this chronic irradiation of blood. Such delay of rejection would be clear evidence of efficacy of the device.

Potential hazards associated with using the irradiators are as follows:

1. There is a surface dose rate up to 50m rad/hr. We are now changing shielding patterns to reduce this and if lower doses prove effective proportionately lower surface doses will exist. Additional shielding can be designed for adjacent skin areas but general shielding would make the units overly burdensome.

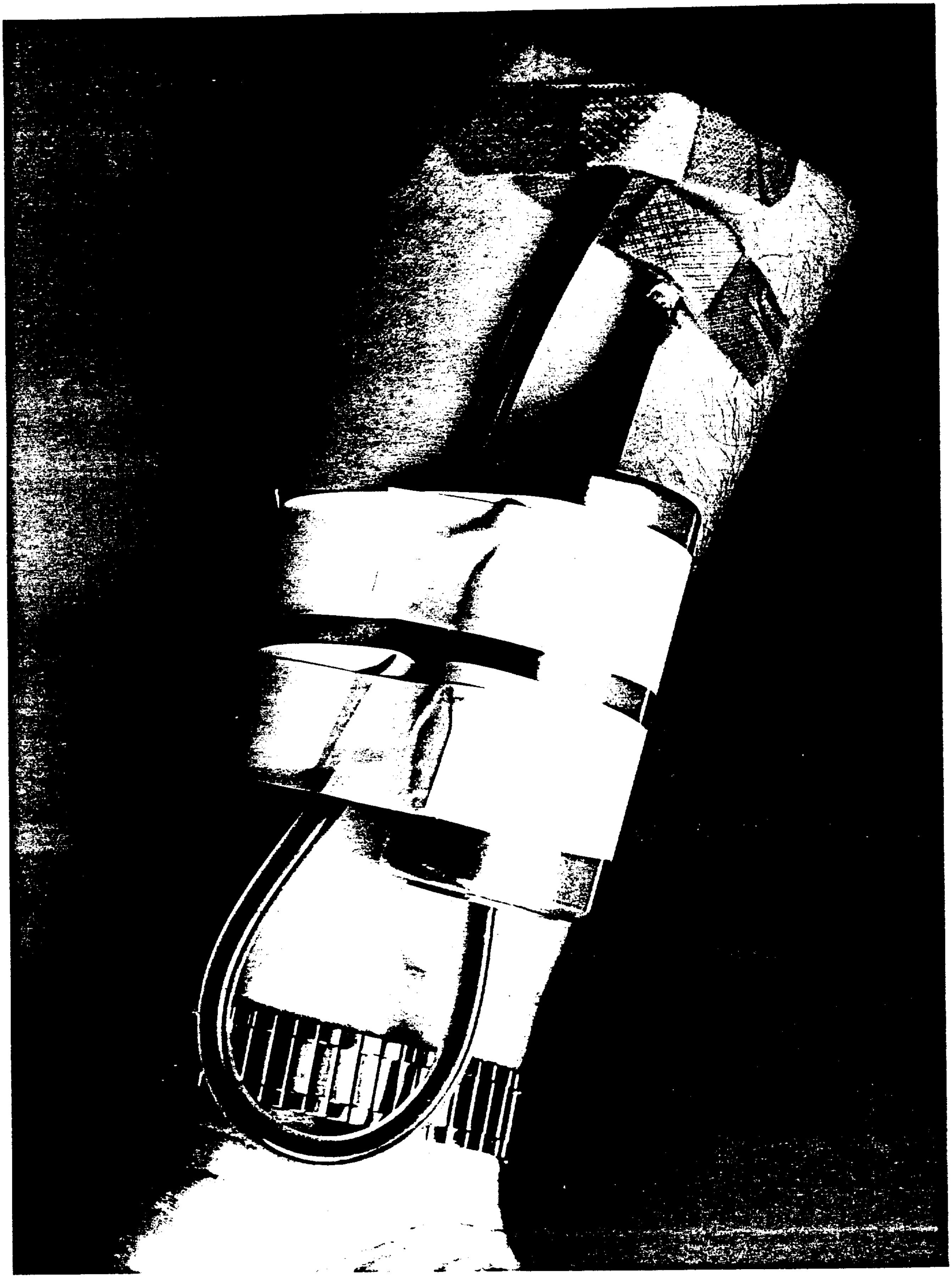
2. Units having no contained fluid emit a narrow end beam of radiation. Thus improper use could results in local exposure. We anticipate a need for a tamper proof seal to eliminate this possiblilty during actual use.

3. A unit could break during use, releasing a limited amount of ^{170}Tm into the blood. We have never experienced this even with the rough treatment from animals. Since the ^{170}Tm is both macro and micro encapsulated only a small fraction of a percent of the material would be released.

4. Units can be destroyed in oxidative temperatures above 500°C. Thus a unit caught in a fire could release ^{170}Tm into the environment. The ^{170}Tm is notvolatile so release would presumably be limited to small particulates entrained in air. ^{170}Tm has a 130 day half life and decontamination with acid solutions tends to be quite effective.

Preliminary discussions with people in licensing (NRC) have indicated no serious difficulties in moving toward licensing the units. However, we have made no formal moves in that direction.

A diagram of the unit and a photo roughly showing how a unit might look on a patient's arm is attached.



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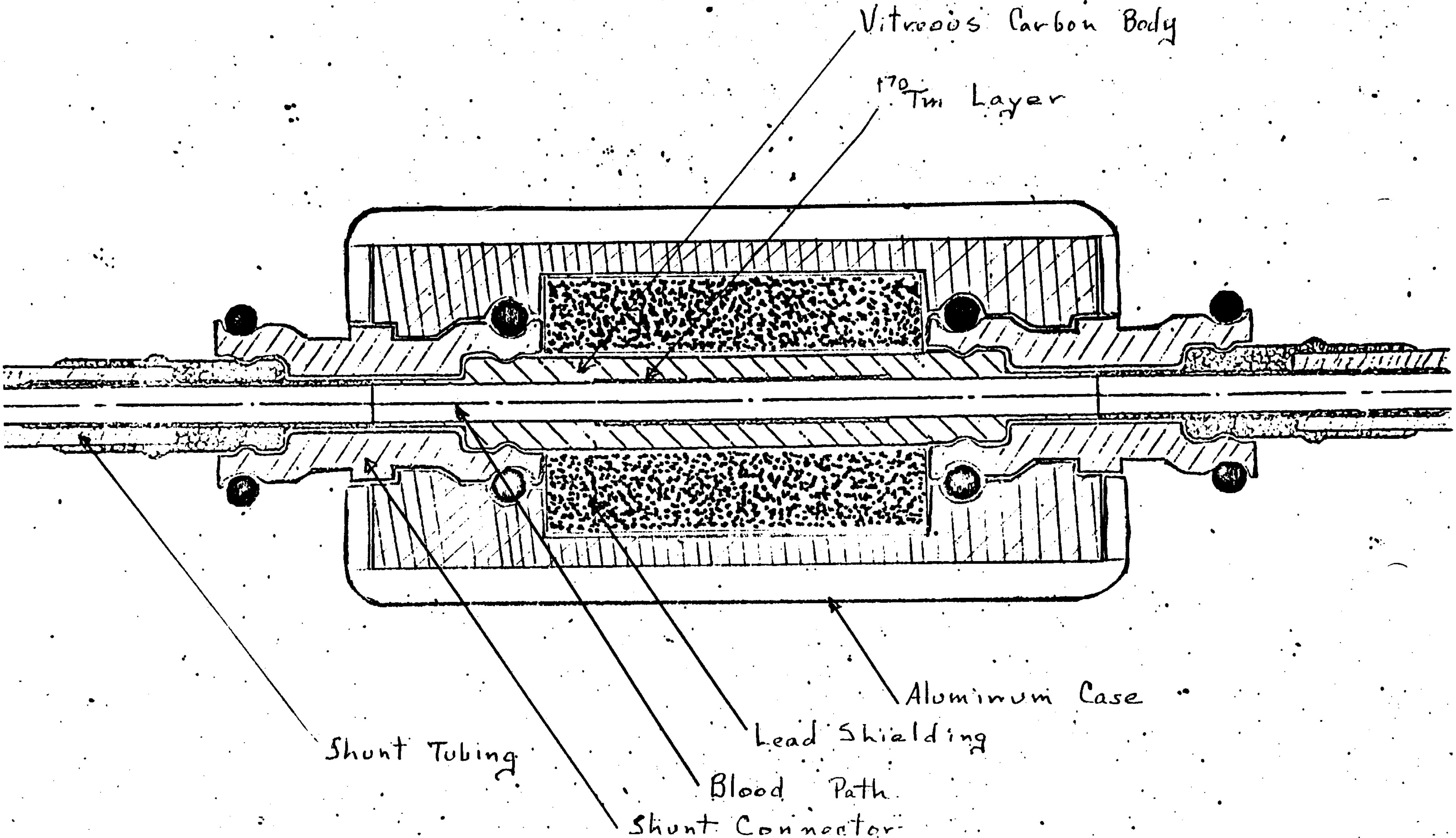
Vitreous Carbon Body
170Tm Layer
Aluminum Case
Lead Shielding
Shunt Tubing
Blood Path
Shunt Connector

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