725541

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 24 March 1971

TO: A. Harrison

FROM: E. P. Cronkite, M.D. E P Cronkite

SUBJECT: CIRC Numbers

The following CIRC #s are inactive. Except for completing old records, they should not be used for identifying patient activity until reactivation is formally approved.

Principal Investigator	CIRC #
Dr. Cronkite	3
	4
	20
	23
	35
	35A
Dr. Dahl	5
	6
	14
	25
Dr. Jesseph	1
Dr. Robertson	9
	10
	16
	28
Dr. Schiffer	22

The Medical Research Center

Brookhaven National Laboratory

Upton, L. I., New York

EPC/ck

cc: CIRC Committee
Mr. Finn
Dr. Dahl

REPOSITORY Records Holding Area Bldg. 494

COLLECTION Committee - Clinical Investigations and use of Radioisotopes

BOX No. 4

FOLDER CIRC #16

1179790

117971

BROOKHAVEN NATIONAL LABORATORY

19

Memo to CIRC FILE #16 Dept.

Per telcon Dr. J.S. Robertson 10/5/66 re proposal:

no activity.

from Anne K. Dept.

FORM NO. 112-A
UPTON, N. Y. 2-57-1500M

Copy of CIRC #16 initially approved by VB o/a 1/22/6[illegible] Sent to CIRC 1/22/[illegible] for committee action Per telcon JSR 10/5/6[illegible] - no activity. [illegible]

FORM FOR INITIATION OR REVIEW OF CLINICAL

INVESTIGATIVE PROGRAMS

(Submit original only to Department Chairman)

A. Title of the proposal: Use of Radiopalladium in Cancer Therapy

B. Sponsoring physician(s): J. S. Robertson

C. Responsible investigator(s): J. S. Robertson

Brief description of the study, including its general goals and purpose, and pertinent information on past studies: (Attach additional sheets if necessary.

This is a collaborative project with Dr. I. M. Ariel of the Pack Medical Group in New York City. For some time he has been developing a "combined thera in which non-resectable cancers are injected directly with radioactive sources at the time of surgery. The proposed uses of Palladium isotopes are part of a search for radiation sources with better radiation and half-life characteristic than those presently in use.

E. Reasons why the investigation(s) are to be performed on human subjects.

Animal studies that have been completed show that injected palladium will remain highly localized at the site of injection and that it is feasible to inject levels of activity that will produce necrosis by irradiation. The test of clinical usefulness is the next stage and requires the use of patients as subjects.

F. Type of patient in which the study is to be done (including approximate number of subjects, if known; special restrictions or requirements; method of obtaining consent; etc.):

The initial studies will be restricted to accessible lesions in patients with established disseminated metastatic malignancies and who have a hopeless prognosis with respect to cureability, but who may be in relatively good condition with respect to not needing intensive nursing care. Consent will be obtained directly from the patient.

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G. 1. Are drugs no in the U. S. Pharmacopoeia (USP) or the NNR being used or contemplated for use? Yes X No ____

2. Is an unusual use of a drug(s) accepted by the USP or NNR contemplated? (An example would be the use of an accepted drug in dosages far exceeding the recommended limits or for purposes distinctly different from the usual indications cited.) Yes ____ No X

3. Are any biological products to be administered that do not bear on their containers or labels notation of approval by the Biological Control Division of the National Institutes of Health? Yes ____ No X

4. Is external or internal radiation other than accepted diagnostic or therapeutic procedures to be administered? Yes X No ____

5. Are any (other) unusual procedures being performed or proposed which in your judgment may entail a special hazard - particularly a hazard above and beyond any imposed by accepted diagnostic and therapeutic measures for that patient? Yes ____ No X

6. Are any radioisotopes to be administered to human beings? Yes X No ____

a. If yes, are the radioisotopes to be used solely within the limits of procedures, specifically described in the USP? Yes ____ No X

Describe the radioisotopic preparation(s):
Colloidal Palladium 103-109 and 111.

b. Or are the radioisotopes to be used only in accordance with a project previously approved by the former Radioisotope Committee of this Department? Yes X No ____

Note the project number: H-67

IF ANY OF QUESTIONS 1 THROUGH 5 ARE ANSWERED AFFIRMATIVELY, a detailed analysis of the potential hazards must be appended, including pertinent bibliographic citations and other relevant information.

IF QUESTION 6 IS ANSWERED AFFIRMATIVELY, a completed supplementary form for Radioisotope Administration to Human Beings must be appended. However, this form need not be filed provided that question 6a or 6b is also answered affirmatively. A separate form must be submitted for each radioisotopic species to be administered.

_____
Sponsoring Physician
James S. Robertson

Committee on Clinical Investigations and Uses of Radioisotopes

Approval recommended _____ Date _____

Disapproval _____ Date _____

_____
V. P. Bond, M. D.
Chairman, Medical Department

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6/25/63
mlk

Investigators: Ariel, Irving M. and Robertson, James S.

Title: Use of Radioactive Palladium (Pd^{103}, Pd^{109}, and Pd^{111}) in Cancer Therapy

Date: Sept. 28, 1960

Project No.: H-67

is approved with the following provisions: 1) only patients with malignant neoplasm (limited life expectancy) will be treated, 2) within the first 24 hours assay of radioactivity in blood specimens, as well as urine and feces, will be regularly performed, and 3) containers of blood and excreta sent to laboratory will be carefully labeled for radioactivity content.

Approved:

Committee on Use of Radioactive Isotopes in Patients:

Walton W. Shreeve

Walton W. Shreeve, M.D., Ph.D.
Chairman

Victor P. Bond

Victor P. Bond, M.D., Ph.D.

Samuel Fine

Samuel Fine, M.D.

Elmer E. Stickley

Elmer E. Stickley, Ph.D.

J. S. Robertson

James S. Robertson, M.D., Ph.D.
Ex Officio

Lee E. Farr

Lee E. Farr, M.D.
Ex Officio

1179794

[redacted]

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 15 September 1960

TO: Isotope Committee

FROM: Dr. Irving M. Ariel
Dr. J.S. Robertson

SUBJECT: Request for use of Pd^{109} in therapy

1. Title: Use of Radioactive Palladium (Pd^{103}, Pd^{109} and Pd^{111}) in Cancer Therapy

2. Investigators: Dr. Irving M. Ariel, Research Collaborator, Park Medical Group, N.Y.C.
Dr. James S. Robertson

3. General Statement:

a. Purpose of study.

Interstitial irradiation by the injection of radioactive sources into inoperable cancers has been practiced for the past forty years. The isotope that has been most frequently utilized for this purpose has been radon gas encased in gold seeds. Originally the radon was encased in glass containers, but the intensely destructive effects of the beta rays penetrating the one-millimeter glass containers made it desirable to filter out the beta rays so that effective irradiation was obtained by only the gamma component of radiation.

The large number of radioactive isotopes now available makes it possible to utilize isotopes with better physical characteristics and better radiologic spectra for the interstitial administration of radiation sources. One of the authors (IMA) has utilized Au^{198}, $Yttrium^{90}$, $CrP^{32}O_4$, and $Iridium^{192}$ in the treatment of patients. These isotopes have been administered either as seeds or as a colloidal suspension. It has been observed that isotopes with a short half-life produce a necrotizing type of biologic reaction in contrast to isotopes with a long half-life, where the slower destructive effect resulting from the radiation is accompanied by a desmoplasia.

Permission is accordingly requested for the use of radioactive palladium, to be administered interstitially in accessible cancers in human beings. This investigation is part of a program for studying the biologic effects of radiations from isotopes having varying half-lives.

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b. Type of patient and proposed procedure.

The initial investigations will be performed upon patients who have disseminated cancer and are therefore hopeless from the standpoint of cure. Initially, patients will be chosen who have an accessible cancer for the interstitial administration of radioactive palladium, the dose depending upon the size of the neoplasm. For example, patients with malignant melanoma who are in good general condition but who have generalized metastases, some of which are subcutaneous, will have the subcutaneous metastases injected with the radioactive isotope. This will be performed as a hospital procedure under local anesthesia. The response to the isotope will be observed clinically, and at varying times after the injection of the isotope the lesions will be excised for histologic analyses. The patients will be hospitalized for a period determined by the clinical status or until the dose of palladium shall have decayed to a level less than 30 millicuries, as recommended by the A.E.C. The fact that palladium is an almost pure beta emitter of limited penetration, and the fact that palladium administered interstitially remains localized would make this isotope a safe one to use from the standpoint of systemic reactions. The fact that the patients selected, at least at the start of this investigation, would be those with a limited life expectancy would make negligible any concern regarding possible effects on the reproductive organs.

On the basis of the dose calculations and the animal studies presented or mentioned below, it is proposed that doses of palladium up to 2 millicuries of Pd^{109} per gram of infiltrated tissue be used. This will deliver a local radiation dose up to 32,000 rad, but only 25 r to tissues 10 cm distant, so the whole-body dose will be kept below 25 r.

c. Pertinent information on past studies.

Nonradioactive palladium (Palladium^{102}) has been injected by the authors of this proposal into the muscles of rabbits. The reaction to the inert palladium was minimal, consisting of a mild lymphocytic reaction with mild granulomatous production. Approximately 50 milligrams of palladium dissolved in 2 milliliters of solution were injected. Harper, Lathrop, Baldwin, Oda, and Kryshtal (1) injected inert palladium black suspension in gelatin into the omentum of rabbits and demonstrated a similar slight reaction. The palladium solution and suspension remain well localized to the site of

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injection, as demonstrated by wet ashing the tissues into which the palladium was injected and the adjacent tissue. This was performed for Palladium^{111}, and Harper et al. demonstrated the localization of palladium black in the leg muscles of a rat when injected in 6 per cent gelatin. Counts of distant organs, both by Ariel and Robertson and by Harper and his colleagues revealed only traces of activity (.003 ± .001 per cent of injected dose/gram of tissue) one, two, and four weeks after administration.

Solutions of Pd^{109} prepared as described above were injected into the leg muscles of 12 rabbits. The histologic effect of Palladium^{109} is essentially that of necrosis with surrounding inflammatory reaction. A dose of 15 millicuries of Palladium^{109}, administered to a volume of approximately 3 grams of tissue, produced a necrotizing but not liquefying degree of necrosis limited to the site of injection. A dose of 150 millicuries produced complete dissolution of the tissue, which dissolution extended to the tissue adjacent to the site of injection. Palladium^{109}, injected into the brains of rats by the Argonne group, produced a sharply delineated necrosis of the brain tissue. Palladium^{103}, injected subcutaneously into rat tissue and into a Walker 256 sarcoma, produced a loss of cellularity with a fibrotic reaction (Argonne Laboratory studies).

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4. Isotope:

a. Nuclear properties of palladium isotopes.

Palladium occurs in nature as a mixture of six isotopes of which three have appreciable thermal neutron capture cross sections for activation by (n,γ) reactions. Because Pd^{109} and Pd^{111} have two isomeric states each, and because some of the decay products are radioactive, a complex mixture of radioactive isotopes having half times ranging from 40 seconds to 17 days is produced, as is indicated in the following table (refs 2 and 3):

Palladium Isotope Activation Reactions

Isotope	Abundance	Cross Section	Product	Half-Life	Decay Mode
A	%		A		
Pd^{102}	0.96	4.8	Pd^{103}	17 d	EC, γ
		(By decay)	Rh^{103m}	57 m	γ
Pd^{104}	10.97	-	-	-	-
Pd^{105}	22.2	-	-	-	-
Pd^{106}	27.3	-	-	-	-
Pd^{108}	26.7	0.26	$Pd^{109}{}_m$	4.75 m	IT
		10.4	Pd^{109}	13.5 h	β^-, γ
		(By decay)	Ag^{109m}	39.2 s	IT
Pd^{110}	11.8	0.21	Pd^{111m}	5.5 h	IT, β^-, γ
		0.05	Pd^{111}	22 m	β^-
		(By decay)	Ag^{111m}	74 s	IT
		(By decay)	Ag^{111}	7.6 d	β^-, γ

Further details of the decay schemes are collected in the following table, copied from the Seaborg table, ref. 2.

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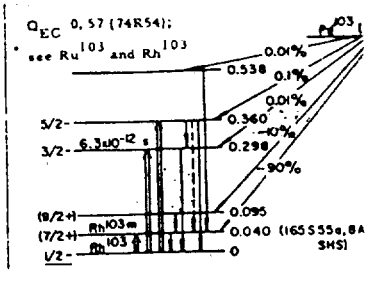
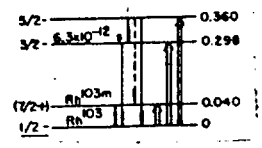
PALLADIUM ISOTOPE DECAY SCHEMES

Pd^{103} and Rh^{103m}

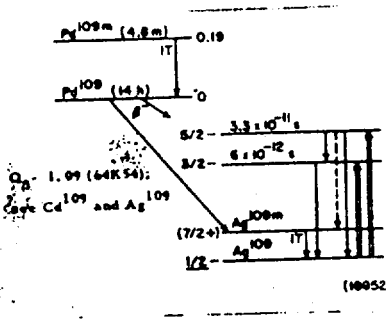
Pd^{103}	17.0 d (16M47, 48B46a, 11M53)	☢ EC (48B46a); A chem, genet (48B46a), chem, excit (36M47); parent Rh^{103m} (48B46a, 53M50a); daughter Ag^{103} (79H54); others (26O53, 37L48, 78S50, 37L50)	EC internal bremsstrahlung endpoint 0.51 scint spect (74R54); γ γ_1 0.0402 (12.1, with Rh^{103m}), γ_2 0.053 (K, L ~1), γ_3 0.065 (10.04), γ_4 0.298 (10.3), γ_5 0.324 (1~0.1, e_K/γ ~10, K/L ~10), γ_6 0.362 (12.1), γ_7 0.498 (10.5) scint spect, spect conv (8A55a, 8A55b, 8A56); γ_1 (0.1%), γ_3 0.065 (4 x 10^{-3} %, coinc with γ_4), γ_4 0.300 (0.012%), γ_6 0.365 (0.07%), γ_7 0.495 (0.01%) scint spect, γ-γ coinc (16S55a). γ_4 0.305 (0.011%), γ_6 0.367 (0.06%), γ_7 0.503 (0.01%) scint spect (74R54); others (36M47, 53M50a, 145M57); see also gammas of Ru^{103} and Rh^{103}	Q_{EC} 0.57 (74R54); see Ru^{103} and Rh^{103}
Rh^{103m}	57 m (33G51f); 58 m (46J56); 56 m (53M50a); 52 m (9F47); 45 m (37W45)	☢ IT (9F44, 37W45); A chem, excit (9F44); chem (33G46a, 33G51f); chem, genet (23S51b); daughter Ru^{103} (23S51b); daughter Pd^{103} (53M50a); others (18H48)	γ 0.0400 (K/L+M 0.2) spect conv, β-γ coinc (38K50, 38K51c, 38K52); 0.0402 (e_K/γ 40, K/L 0.09) spect conv (8A55a); 0.0404 (e/γ very large) spect conv (53M50a); 0.0396 (K/L 0.1) spect conv (10C52); 0.040 (K/L 0.18) spect conv (73D55); others (8A53a, 79S50, 37W45, 9F47, 46J56)	Q_{IT} 0.040 (SHS); see Ru^{103}
Rh^{103}		% 100 (57C43);	γ Coulomb excitation (in Rh^{103});	

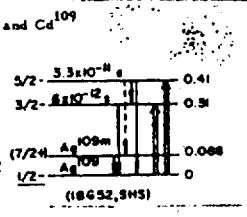




Pd^{109m} Pd^{109} and Ag^{109m}

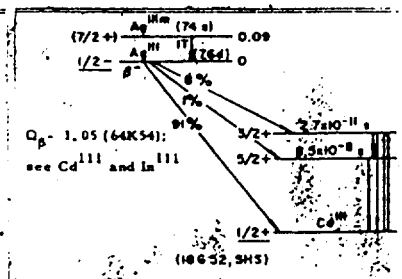
Pd^{109m}	4.75 m (15S57a); 4.7 m (23S57); 4.8 m (9F52a)	☢ IT (31K51, 9F52a); B n-capt (31K51); excit, cross bomb, n-capt (9F52a); n-excit, sep isotopes (20TS58)	γ 0.188 (e_K/γ 0.6) scint spect (15S57a); 0.188 scint spect (23S57); 0.170 scint spect (20TS58); 0.173 scint spect (31K51); 0.160 (e/γ ~0.6) (9F52a)	
Pd^{109}	13.5 h (23S57); 13.6 h (11M53); 13.1 h (25W48); 13 h (39K37, 77S51, 38K52); 14.1 h (60M46); 14 h (92D57)	☢ β^- (39K37); A n-capt (12A35); chem, excit (39K37); chem, mass spect (37R46, 67B49a); others (12P48, 60M48, 25W48, 22K54, 4B47, 9O49, 50H51, 4F38b, 29K47a, 37L50, 11G49, 21T51, 61S48, 32K48); [daughter Rh^{109}] (77S51); parent Ag^{109m} (24S41, 7S49b, 77S51)	β^- 1.02 spect (96M54), 1.03 spect (23S57), 0.95 spect (7S49b, 38K51c, 38K52), others (22H46, 39K37, 77S51); γ 0.307, 0.320, 0.325, 0.412, 0.429, 0.448, 0.55, 0.64, 0.77 (all gammas weak) scint spect, γ-γ coinc (23S57); 0.314 (0.02%), 0.412 (0.02%), 0.64 (0.02%), 0.77 (0.02%) (20K57a); 0.305 (0.07%), no 0.410 γ scint spect (47W57). with Ag^{109m}: 0.087 (e/γ >11, K/L+M 1.3) spect conv (7S49b); others (77S51, 70D57a); see also gammas of Ag^{109m} and Cd^{109}	Q_{β^-} 1.09 (64K54); see Cd^{109} and Ag^{109}
Ag^{109m}	39.2 s (16B46c, 16B47); 40 s (40W51, 2H41b, 37W45b, 20TS57)	☢ IT (2H41b); A chem, genet (2H41b); daughter Pd^{109} (24S41); daughter Cd^{109} (2H41b, 16B45c, 2H46); others (9F44, 31F41, 24T45)	γ 0.0875 spect conv (10C50b); 0.0879 spect conv (32J53); 0.0875 (e_K/γ 10.3, K/L+M 0.80) scint spect, spect conv (47W54b, 47W57); 0.0877 (e/γ 14, K/L+M 0.84) spect conv (96M54); ~0.087 (e_K/γ 12, K/L+M 0.85) spect conv, scint spect (114B53); others (96H54, 8A53b, 34N53b, 38K52, 34H52, 7S49b, 2H46, 16B47, 32K57); see also gammas of Pd^{109} and Cd^{109}	see Pd^{109} and Cd^{109}
Ag^{109}		% 48.65 (24W46);		





Pd^{111m} Pd^{111} Ag^{111m} and Ag^{111}

Pd^{111m}	5.5 h (66M52, 92D57)	☢ IT 75%, β^- 25% (66M52); A chem, genet (66M52, 92D57); parent Ag^{111} (66M52, 92D57)	γ 0.17 scint spect (66M52, 66M57) β^- 2.3 or less	
Pd^{111}	22 m (66M52); 26 m (24S41)	☢ β^- (39K37); A n-capt (12A35); chem, genet (24S41); parent Ag^{111} (39K37, 24S41); parent Ag^{111m} (20TS57); others (2S47, 37L50, 5N40a, 92D57)	β^- 2.15 spect (66M52); 3.5 abs (70B43b)	
$_{47}Ag^{111m}$	74 s (20TS57); others (80S52)	☢ IT, no β^- (lim 1%) (20TS57); B chem, genet (20TS57); daughter Pd^{111} (20TS57)	γ ~0.087 abs conv (20TS57)	
Ag^{111}	7.6 d (61S51c); 7.4 d (68F57); 7.5 d (17J50, 39K37, 1P38); others (29K47a, 4ZH47, 23D49a, 37L50, 11G49, 7N49a, 6O48, 61S51c, 5N40a, 21T51, 28F51)	☢ β^- (39K37); A chem, excit (39K37); chem, excit, cross bomb (1P38); daughter Pd^{111} (39K37, 24S41, 17J50); daughter Pd^{111m} (66M52, 92D57); I 1/2 atomic beam (98W56, 73L54). μ -0.145 atomic beam (98W56, 98W55); 0.144 atomic beam (73L54); see also μ of Cd^{111}	β^- 1.04, 0.79 (coinc with γ_1), 0.69 (coinc with γ_2) (89R58); 1.04 (91%), 0.80 (1%), 0.70 (8%) spect (17J50); 1.06 spect (66M51, 53M50b); 1.1 (94%), 0.7 (6.5%) abs (78S50); average energy of β^- 0.38 ion ch (195B53); γ γ_1 0.243 (e/γ <0.08), γ_2 0.340 (e/γ ~0.015) (γ_2/γ_1 ~6) spect, spect conv, β-γ coinc, γ-γ coinc (17J50); γ_1: $t_{1/2}$ 1.0 x 10^{-7} s delay coinc (13E51c); others (66M51a, 78S50); see also gammas of Cd^{111m} and In^{111}	Q_{β^-} 1.05 (64K54); see Cd^{111} and In^{111}



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b. Source and preparation.

Palladium^{109} is obtained by activation at the Graphite Research Reactor. Based upon the above information, activation at a thermal neutron flux of 10^{13} n/cm^{2}sec yields specific activities calculated as follows: First generation products were calculated from the usual formula: $SA_1 = \frac{1.64\ \phi\ \sigma f}{10^{11}\ A}(1 - e^{-\lambda t})$, where SA is the specific activity, ϕ the flux, σ the cross section, f the isotopic abundance, A the atomic weight of the target isotope, λ the decay constant of the product, and t the in-pile time.

For radioactive daughter products, integration of $\frac{dN_2}{dt} = \lambda_1 N_1 - \lambda_2 N_2$, where N_1 and N_2 are the numbers of radioactive atoms of parent and daughter species, leads to $SA_2 = \frac{1.64\ \phi\ \sigma f}{10^{11}\ A}\left[1 - \frac{\lambda_2}{\lambda_2 - \lambda_1} e^{-\lambda_1 t} + \frac{\lambda_1}{\lambda_2 - \lambda_1} e^{-\lambda_2 t}\right]$

(Only in-pile time, t, is considered here):

Palladium Activation

Isotope	Half-Life	Specific Activity for $\phi = 10^{13}$ n/cm^{2}sec			
		In-pile activation time			
		12 hr mc/g	1 day mc/g	2 days mc/g	Saturation mc/g
Pd^{103}	17 d	1.5	3.0	5.9	75.5
Rh^{103}	57 m	1.5	3.0	5.9	75.5
Pd^{109m}	4.75 m	110	110	110	110
Pd^{109}	13.5 h	1980	3050	3940	4320
Ag^{109m}	39.2 s	1980	3050	3940	4320
Pd^{111m}	5.5 h	28.8	35.1	36.8	36.9
Pd^{111}	22 m	37.1	43.6	45.6	45.7
Ag^{111m}	74 s	37.1	43.6	45.6	45.7
Ag^{111}	7.6 d	0.8	2.6	6.2	45.7

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The presence of the Pd^{103} and Pd^{111} radioisotopes is not necessarily undesirable in therapeutic applications, as a mixture of dose rates may be advantageous. As will be shown, however, in the proposed method of use, the radiation contribution from these "contaminating" isotopes is not important.

$Palladium^{109}$ is obtained from the reactor in a 4-ml quartz container containing from 100 to 400 mg of palladium which has an activity varying from 200 to 800 millicuries, depending upon the in-pile time and the amount of target material used. The material is dissolved in aqua regia and the solution brought to neutrality by the addition of concentrated sodium hydroxide. The solution is maintained at a slightly acid reaction inasmuch as if it becomes slightly basic, a precipitate of palladium chloride forms. If it is desired to inject the material as larger-sized colloidal particles, the palladium can be precipitated as palladium black by the administration of formic acid to the above solute. Palladium metal can also be prepared as needles with an outside diameter of 0.45 millimeters that can be activated and administered interstitially.

By waiting for radioactive decay of Pd^{109} to a suitable level, it will contain a higher proportion of $Palladium^{103}$ and Ag^{111}. The administration of the material would then have the combined effect of a short-lived isotope and an isotope with a longer half-life.

The availability of palladium as a salt in solution, colloidal suspension, and as seeds or needles offers satisfactory physical and chemical characteristics for interstitial application. In the initial studies, the solution form will be used.

c. Assay and calibration.

The technique of assaying Pd^{109} is made difficult by the complexity of the mixture obtained, and is still being developed. The gamma activity will be assayed with the use of the 100-channel pulse-height analyzer. The Pd^{109} β activity will be determined by appropriate dilution and counting of an aliquot evaporated on a planchet in a shelf GM counter

d. Sterility and pyrogenicity control.

Sterility of the material to be infiltrated will be achieved by autoclaving in a rubber-topped dispensing vial.

None of the materials used in the preparation is known to have pyrogenic properties, and in view of the short half-life of the principal isotope, it is not feasible to test for pyrogenicity prior to use to a given preparation.

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5. Radiation Dose Estimation:

Because of the complexity of the isotope mixture and the manner in which it is to be used, it is very difficult to arrive through calculations at a meaningful estimate of the radiation dose which will be attained when radioactive palladium is infiltrated into a tumor mass. An estimate is necessary, however, to provide a working basis for deciding how much activity to use.

Obviously, if the activated material is used within a few hours of its removal from the pile, the chief source of radiation will be Pd^{109} and its decay product Ag^{109m}. Unfortunately the decay scheme of Pd^{109} is not too well established. Gamma rays of up to 0.305 MeV are seen, but in only about 0.1% of the disintegrations. For the present purposes it may be assumed that Pd^{109} decay involves only β^- emission ($\bar{E}$ = 0.34 MeV) followed by emission of an 88 kev gamma ray in the Ag^{109m} to Ag^{109} transition. Using the β^- dose formula 17, p. 828, ref. 4, we have $D_\beta = (73.8)(0.34)(\frac{13.5}{24}) = 14.1$ rad/μc/g. For the gamma radiation, the graph on p. 757, ref. 4, indicates a Γ factor of 0.4 r-cm^2/mc-hr. Inserting this value in eq 88, p. 861, ref. 4, and assuming a geometry factor of 22.3 (corresponding to uniform distribution in a cylindrical mass 6 cm diam. and 5 cm long, p. 858, ref. 4, gives $\bar{D}_\gamma = (0.0346)(0.4)(22.3)(\frac{13.5}{24}) = 0.174$ rad/μc/g. Thus the γ dose is relatively negligible locally, although it may be important in considerations of the irradiation of distant sites. As an example, let us assume that we wish to deliver 30,000 $\bar{\beta}^-$ rad to a tumor. This requires a concentration of $\frac{30,000}{14.1} = 2124$ μc/g, and if the mass infiltrated is 141 grams, 300 mc are needed. Regarding this as a point source, a point 10 cm away would receive $(300)(0.4)(1.44)(13.5)(10^{-2}) = 23$ r of gamma irradiation.

For Pd^{103} the highest possible contribution to the local dose may be calculated by assuming that the entire Q value of 0.57 MeV plus the 0.04 Mev from Rh^{103m} decay is absorbed locally. (See ref. 5.) Using the β^- dose formulas (because they assume total local absorption of the emitted energy) 10 c, p. 824 and 17, p. 828, ref. 3, we have

$$R = (51.2)(0.61) = 31.2 \text{ rad/day/}\mu\text{c/g} \quad \text{initially}$$

$$D = (73.8)(0.61)(17) = 765 \text{ rad/}\mu\text{c/g}$$

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In terms of 1 μc of Pd^{109}/g, however, the contribution from Pd^{103}, assuming that freshly activated, saturated material is used, is $(765)(\frac{75.5}{4320}) = 13.4$ rad, or about the same as the dose from Pd^{109}. In material activated for a shorter time, the relative contribution from Pd^{103} will be less; with 12 hours activation it is only $(765)(\frac{1.5}{1980}) = 0.58$ rad, for 1 day it is 0.75 rad and for 2 days, 1.5 rad.

For Pd^{111m} and its chain of products we may use the 48-hour activation time values (instead of the saturation values) to avoid overestimating the contribution from Ag^{111}. There are then a 2.3 MeV (or less) β^- from Pd^{111m} in 25% of $\frac{36.8}{3940}$ Pd^{109} disintegrations, and from Ag^{111} there are 3 β^-'s, the relative weightings being (1.04)(91%) + (0.80)(1%) + (0.70)(8%), all occurring in $\frac{6.2}{3940}$ Pd^{109} disintegrations. The β^- dose is then:

$D_\beta = 73.8\ \bar{E}\ C = 0.169$ rad/μc Pd^{109}/g from Pd^{111m} and Pd^{111}, and 0.280 rad/μc Pd^{109} g from Ag^{111}.

Since gamma rays are emitted in only 9% of the Ag^{111} disintegrations, it is apparent that the γ dose from this source is negligible, relative to that from Pd^{109}.

In summary, assuming 2 days' activation time, infiltration of Pd^{109} in a concentration of 1 μc/g into a mass 6 cm diam. and 5 cm long will result in the following local radiation doses:

Pd^{109}	14.3 rad
Pd^{103}	1.5 rad
Pd^{111}	0.5 rad

The whole-body and gonadal dose will be kept below 50 r by using less than 500 mc of Pd^{109} localized in the tumor mass.

6. Health Physics Aspects:

a. Hazards to others.

During the first two days or so after administration of Pd^{109} there will be sufficient external gamma irradiation to warrant isolation of the patient. Necessary attention by the nursing staff will be permissible, but the nurses' time in the patient's immediate vicinity must be limited to a minimum during the first 24 hours.

b. The animal experience indicates that radioactivity getting into the excreta will not be a problem. Initial (first 48 hours) urine specimens will be collected and checked for radioactivity, however.

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