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CALIFORNIUM-252 RADIOTHERAPY SOURCES FOR INTERSTITIAL AFTERLOADING

MASTER

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ABSTRACT

Californium-252 neutron sources for interstitial afterloading were developed to investigate the value of this radionuclide in cancer therapy. Californium-252 seed assemblies contain essentially point sources of ^{252}Cf permanently sealed on 1-cm centers within a flexible plastic tube.

The seed assemblies are fabricated with remotely operated, specially designed machines. The fabrication process involves the production of a Pt-10% Ir-clad wire with a $^{252}Cf_2O_3$-Pd cermet core. The wire is swaged and drawn to size, cut to length, and welded in a Pt-10% Ir capsule 0.8 mm in diameter and 6 mm long. Each seed capsule contains approximately 0.5 microgram of ^{252}Cf.

Because the effective half-life of ^{252}Cf is 2.6 years, the seed assemblies are not disposable and must be reused until their activities have decreased to unsuitable levels. The flexible plastic components must therefore have sufficient resistance to radiation damage to survive the neutron-plus-gamma radiation from ^{252}Cf. On the basis of accelerated irradiation tests with a large ^{252}Cf source, a recently developed fluoropolymer, "Tefzel" (trademark of E. I. du Pont de Nemours and Company) has adequate radiation resistance for this application.

Californium-252 seed assembly systems are loaned by the United States Energy Research and Development Administration for clinical investigations under a protocol of the Radiation Therapy Oncology Group, U. S. National Cancer Institute.

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INTRODUCTION

Californium-252 is a man-made radioisotope that provides a small, intense source of neutrons, readily adapted to cancer therapy. One microgram of ^{252}Cf emits 2.3×10^6 neutrons per second at a calculated average energy of 2.3 Mev[1]. Because of its high specific neutron activity, californium-252 is ideally suited for internal radiation therapy by the interstitial implant technique. In this technique, the source is inserted directly into the cancer by means of a plastic tube sutured into the tumor[2].

The present system for ^{252}Cf interstitial implants (Fig. 1) resembles the "seed-in-ribbon" system developed for ^{192}Ir by Henschke, Hilaris, and Mahan[3]. Each seed assembly is essentially a series of point sources or "seeds" of ^{252}Cf (each 0.5 μg), spaced 1 cm apart in a radiation-resistant, flexible plastic tube. Because the half-life of ^{252}Cf is 2.6 years compared to 74 days for ^{192}Ir, the ^{252}Cf seed assemblies may be re-used until the treatment time becomes excessive. A service life of at least two years is anticipated.

This paper describes the design and fabrication of the ^{252}Cf seed assemblies that are now being supplied by the U. S. Energy Research and Development Administration, Savannah River Operations Office, Aiken, S. C., for comparison with gamma radiation in the treatment of cancer under a protocol developed by the Radiation Therapy Oncology Group, National Cancer Institute[4].

DESIGN AND FABRICATION OF THE ^{252}Cf "SEED" CAPSULE

The capsule wall was designed to limit the undesirable beta radiation from ^{252}Cf to a level acceptable to the radiotherapist. The thickness of dense (21.5 g/cm^3) Pt-10% Ir alloy was selected to limit the beta-plus-gamma dose rate to one-third of the neutron dose rate at 0.5 cm from the source. At the same time, the outer diameter of the seed was kept as small as possible, so that the outer diameter of the completed system would be no larger than 1.6 mm, the diameter of a 16-gauge surgical needle. The nominal seed diameter is 0.8 mm and the overall length is 6 mm (Fig. 1).

To ensure that no ^{252}Cf is included in the closure welds and that the ^{252}Cf core is centered in the capsule, 1-mm long Pt 10% Ir end plugs are positioned and welded at both ends.

Fabrication of the encapsulated seed

The ^{252}Cf seed assembly described in this paper was made possible by the development of a ^{252}Cf-containing wire that can be cut to precise length. The wire, clad in Pt-10% Ir alloy, has a Pd-Cf_2O_3 cermet core. In the core, each particle of Cf_2O_3 is enclosed in a matrix of ductile palladium, which thus provides effective containment of all the ^{252}Cf except that which is exposed at the ends of each cut segment. The effective containment provided by the clad core adds to the safety of the singly encapsulated seed design.

The entire process (flowsheet in Fig. 2) is performed remotely in six shielded cells by machines specially designed for operation with master-slave manipulators[5]. To observe the very small components, out-of-cell telephoto television cameras and optical telescopes are focused through the waterfilled windows.

Composite billet

A composite billet (Fig. 3) contains a Pd-Cf_2O_3 core gold-brazed in a Pt-10% Ir container, 0.76 cm dia x 3.56 cm long. The core is prepared by the deposition of palladium on a fine precipitate of ^{252}Cf oxalate in an aqueous system[6].

Swage and draw

The clad wire is made by swaging and drawing. The wire provides a source form that can be subdivided with a minimum of contamination. The swaging operation requires only five reductions and one anneal at 1100°C to reduce the billet from 7.6 mm to 2.5 mm. The drawing operation requires approximately 44 passes, which reduces the cross-sectional area by 10% per draw. Four annealing cycles at 1100°C are required during the drawing operation. A cross-section of a finished wire (Fig. 4) reveals a reasonably symmetrical core.

The swager-draw bench (Fig. 5) was designed specifically for this process. A Model NF Fenn swager (The Fenn Manufacturing Co., Newington, Connecticut) was modified for remote operation. The swager feed system is a pneumatic gripper mounted on a traverse mechanism capable of variable speed and thrust forces. The traverse mechanism consists of a Roh'Lix (Barry-Wright Corp., Watertown, Massachusetts) actuator system that converts rotary motion to linear motion on a smooth shaft. The linear speed is controlled by the speed of the rotating shaft. The thrust force is controlled by the compressive force applied to the shaft by the air cylinders on the Roh'Lix actuators.

The drawing operation uses the same traverse mechanism to pull the draw dies over the wire. Nine draw dies are mounted on a rotary index that is connected to the traverse mechanism by a latching device. The rotary index has an open position to permit pointing the wire with the swager. The wire is held by a second pneumatic gripper that is pivoted into operating position in front of the swager. Both the swager spindle and the grippers have hollow bores to permit wires of infinite length to be processed.

Precision cut

The 0.35-mm-diameter drawn wire is cut into lengths of 4.0 ± 0.10 mm and placed into a Pt-Ir capsule having a diametrical clearance of approximately 0.10 mm. A precision length cutter and transfer machine (Fig. 6) was designed to cut the desired lengths and to transfer the pieces to a capsule for loading.

Loading and welding capsule

Seed capsules are made from 0.8-mm-diameter Pt-10% Ir tubing, which is visually inspected with a 20X-binocular microscope for metallurgical defects. Prior to transfer to the shielded cell, one end of the capsule is welded and inspected to assure that the welded end plug is 1.0 mm long. These capsules are mounted in a special collet for manipulator handling during the loading and welding operations. The collet is equipped with an adjustable depth stop and a copper heat sink to control capsule melting during the welding operation (Fig. 7).

The loading and welding machine consists of two independently operated XYZ stages mounted on a common platform. One stage contains a pneumatic collet holder to support and position the capsule. The other stage supports and positions a pneumatic cutter.

The first stage positions the capsule collet under the source wire which is presented by the precision-length cutting machine. An out-of-cell television system providing a 5:1 magnification of the positioning operation is observed by the operator watching a video monitor (Fig. 8). A mirror is positioned 2 cm from the capsule and wire. The capsule and wire are observed on the video monitor as direct and mirror images. When the capsule and wire are lined up in both images, the capsule is raised up around the wire, and the precision cutter and transfer device releases the wire permitting it to fall into the capsule.

While the transfer device is still extended with the gripper open, a length of Pt-Ir plug wire is placed in the jaws with the master-slave manipulators. The plug wire is loaded into the capsule as described in the previous paragraph. The second stage is then driven over the loaded capsule, positioning the cutter to cut off the excess capsule and plug wire. The cutter blades are designed to leave 0.25 mm of the capsule protruding above the flat surface of the copper heat sink. This protrusion was determined to be necessary for a good closure weld.

Low-current plasma-arc welding is far superior to tungsten-inert-gas (TIG) welding for making the closure weld on ^{252}Cf seeds. In the plasma-arc process, the arc is first established between a nonconsumable tungsten electrode and a constricting orifice (nozzle). During welding, the plasma of hot gas is transferred to the workpiece for 6 sec at 5 amps. Distance between the nozzle and workpiece is approximately 6-12 mm. The resulting arc is very stable, particularly at this low current; the arc length is not critical, and contamination of the tungsten electrode with Pt-Ir alloy is eliminated. With conventional TIG welds, arc stability, spacing, and electrode contamination present difficult operating problems.

Leak testing

An acid-vacuum leach test was developed for detecting imperfect seeds caused by either faulty welds or defects in the Pt-10% Ir tube walls. Each seed is tested individually by measuring the alpha activity of an acidic penetrant. The seeds are first decontaminated in an ultrasonic bath in two successive rinses of 4M HNO_3 followed by a water rinse. A seed is next immersed in 3 ml of 4M HNO_3; the pressure is reduced to 130 mm Hg for 3 minutes and then returned to atmospheric pressure. The cycle is repeated a total of three times, and the seed then remains in the acid for 16 hours. One ml of the acid is evaporated to dryness, and its alpha activity is determined by counting for one minute in an alpha scintillation counter. If the activity of the acid is more than 10 dis/min above background, the seed fails the test. An activity of 10 dis/min corresponds to 0.0045 nanocurie of ^{252}Cf. Because we analyze a 1-ml sample from the 3 ml of acid used to leach the sample, the maximum allowable surface activity is then 3 x 0.0045 or 0.0135 nanocuries per seed.

SOURCE ASSAY

Each seed is individually calibrated in a neutron counter to establish ^{252}Cf content. The counter consists of a cubical polyethylene moderator 60 cm on a side in which 18 BF_3 tubes are mounted in a circle 18-cm in diameter. The ^{252}Cf seed, surrounded by an 11.5-cm-diameter Pb shield, is located precisely in the center of the array of BF_3 tubes. The Pb shield protects the BF_3 counters from the ^{252}Cf gamma radiation, and the polyethylene moderator thermalizes the ^{252}Cf neutrons, which are then detected by the BF_3 counters operated in the ionization mode. The output signals from the BF_3 counters are summed and fed to a digital picoammeter. The system can readily detect 10 nanograms of ^{252}Cf, and will measure up to 200 micrograms. The precision of a 1-microgram ^{252}Cf source assay is ±1.0%.

The ^{252}Cf is supplied in sets of approximately 180 seeds each containing a nominal 0.5 microgram of ^{252}Cf. Assay of each seed is required to be within ±5% of the mean of the set, which requires that seeds be selected individually after assay. Because the precision of the counter is ±0.1%, the production control band is ±0.4% around the mean. Assay plots of individual seeds (Fig. 9) from two wires show typical source strength distributions. Each seed contains the same length of core wire. The concentration of ^{252}Cf in the core varies from wire to wire. For example, wire no. 2056 was essentially uniform along its entire length. The ^{252}Cf content of wire no. 2057 was high at both ends. The source strength of the seeds is controlled by the wire diameter.

SEED ASSEMBLIES

^{252}Cf seed assemblies for interstitial afterloading are prepared by mounting from 3 to 7 individual ^{252}Cf seeds spaced 1 cm apart in a radiation-resistant plastic tube. An essential feature of the ^{252}Cf seed assembly is the selection of a plastic that will tolerate the ^{252}Cf radiation. All organic materials are subject to radiation damage by exposure to neutrons and gamma rays, both of which are emitted by ^{252}Cf. The calculated neutron-plus-gamma dose at the interface between a 0.5 µg ^{252}Cf seed and the plastic sheath is $\sim 10^4$ rad/day.

A recently developed thermoplastic fluoropolymer, "Tefzel"*(ethylene-tetrafluoroethylene), was selected for the plastic components of the ^{252}Cf seed assembly. "Tefzel" is available as heat-shrinkable tubing and can be melt-sealed and welded. "Tefzel" is tough and has medium stiffness and excellent resistance to abrasion. "Tefzel" is inert to strong mineral acids, inorganic bases, halogens, and metal salt solutions; carboxylic acids, anhydrides, aromatic and aliphatic hydrocarbons, alcohols, aldehydes, ketones, ethers, esters, chlorocarbons, and classic polymer solvents have little effect on "Tefzel." "Tefzel" is affected to various degrees by very strong oxidizing agents such as nitric acid, by organic bases such as amines, and by sulfonic acids at high concentrations near their boiling points.

Radiation testing

An accelerated radiation test was devised in which dummy seed assemblies were exposed in direct contact with a large ($\sim$5 mg ^{252}Cf) neutron source for known times, then were removed and subjected to a bend test more severe than would be expected in service (Fig. 10). An exposure of 1 day in the test fixture is approximately equal to 64 days' service in the ^{252}Cf seed assembly.

* Trademark of E. I. du Pont de Nemours and Co.

The most recent tests show that the "Tefzel" retains adequate flexibility (50 reverse bends around a 0.63-mm mandrel followed by 100 reverse bends around a 0.38-mm mandrel after a dose of 2.0×10^7 rads, neutron-plus-gamma, equal to a service life of ∿2000 days. Longer exposures (2.2×10^7 rads) caused the "Tefzel" to develop a fissure at the point of bending after seven reverse bends around the 0.63-mm mandrel. In no test did the "Tefzel" show typical brittle behavior.

Stacking seeds and spacers in tubing

The ^{252}Cf seed assembly is made by stacking seeds and "Tefzel" spacers in a heat-shrinkable "Tefzel" tube with wall thickness of ∿0.11 mm. The assembly is placed into an oven to shrink the tube down over the seeds and spacers, firmly locking them in position. Plugs of the same thermoplastic are located in both ends of the assembly and are melt sealed to maintain confinement.

A stacking and transfer machine (Fig. 11) was designed for the stacking operation. The machine is an electro-pneumatic device containing two vibratory parts feeders which present the seeds and plastic spacers alternately to a pivoting pneumatic gripper which takes the piece and presents it to the plastic tube for loading. The plastic tube is positioned in an XYZ stage using the television camera and video monitor previously described.

Prior to shipment, the completed and sealed assembly is autoradiographed to verify the number and spacing of seeds. A standard inventory of 41 seed assemblies (Fig. 12) is prepared for members of the ^{252}Cf medical evaluation program. A typical inventory contains 90-100 micrograms of ^{252}Cf.

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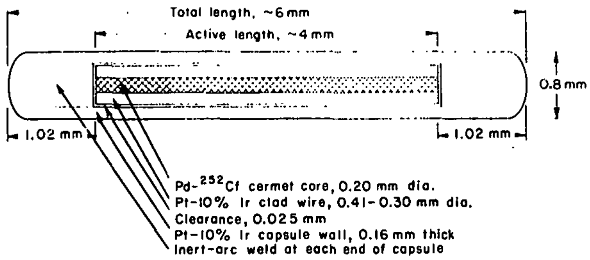
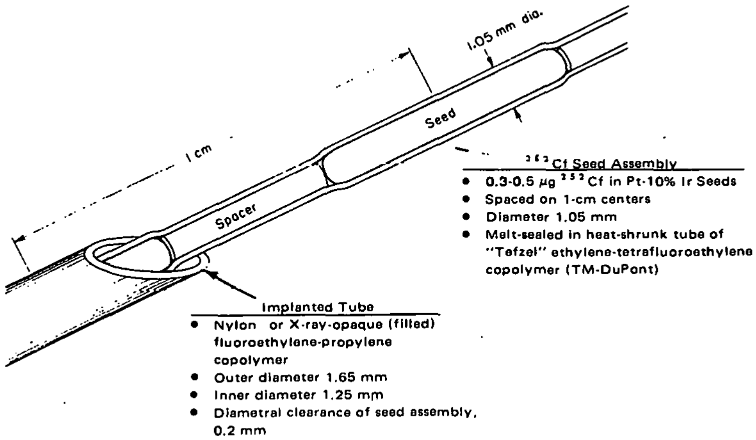
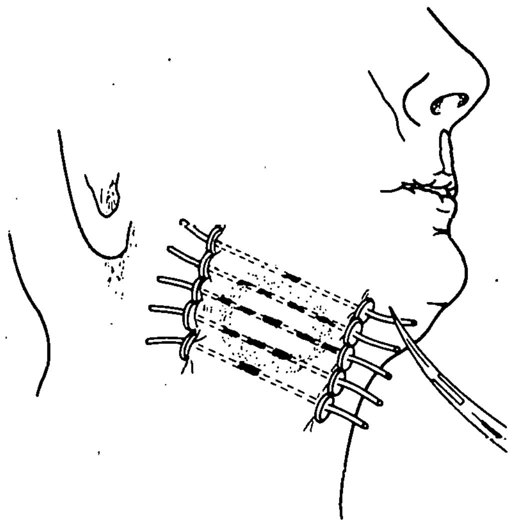
LIST OF FIGURES



^{252}Cf Neutron Source (Seed) ALC-P4C



^{252}Cf Interstitial Implant System



^{252}Cf Seed Assembly Inserted in Implanted Tubes

Fig. 1. ^{252}Cf Medical Source

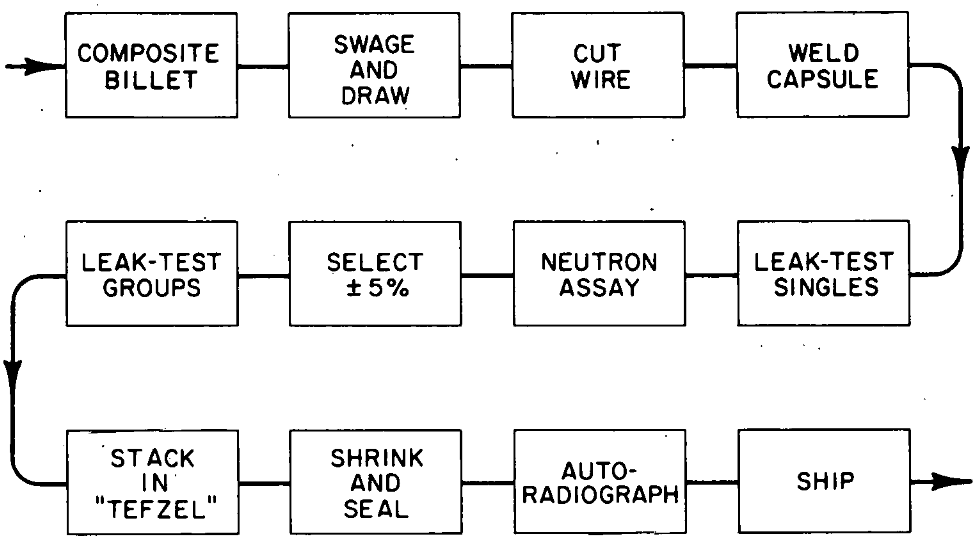


FIGURE 2. Flowsheet for Fabrication of ^{252}Cf Seed Assemblies

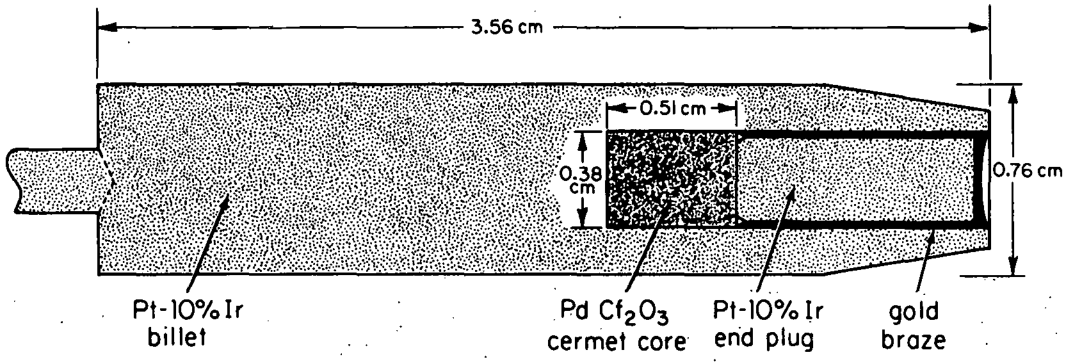


Fig. 3. Composite Billet, Longitudinal Section

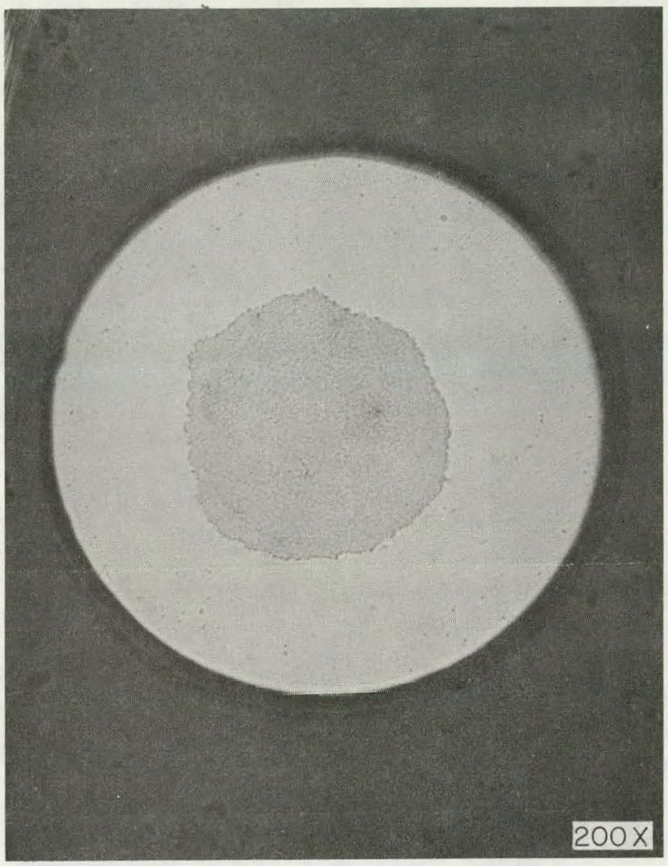


Fig. 4. Cross Section of 0.35 mm-dia, Pt-10% Ir-Clad Wire Containing $^{252}Cf_2O_3$-Pd Cermet Core

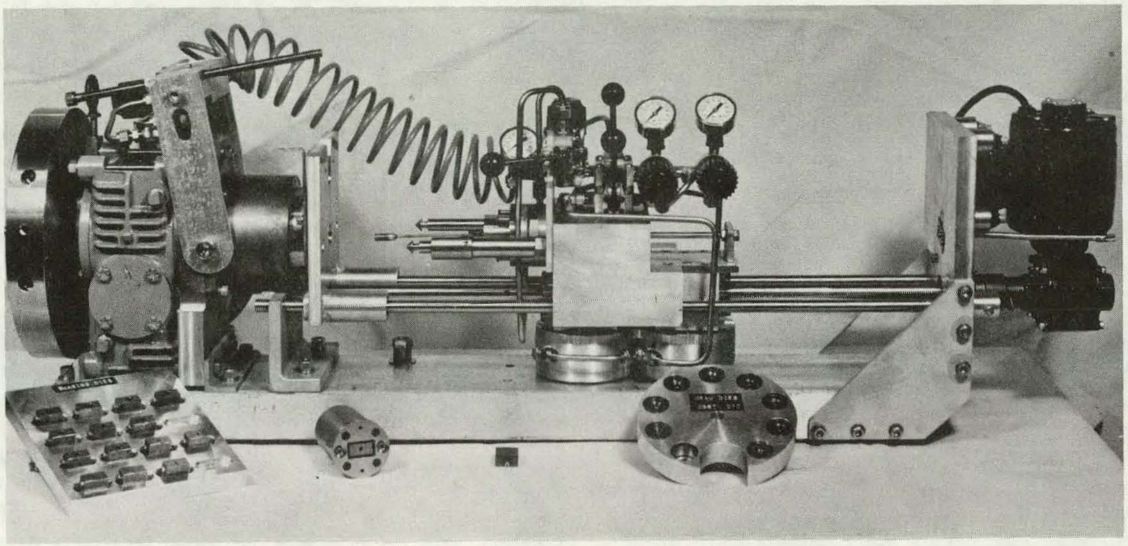


Fig. 5. Swager-Drawbench

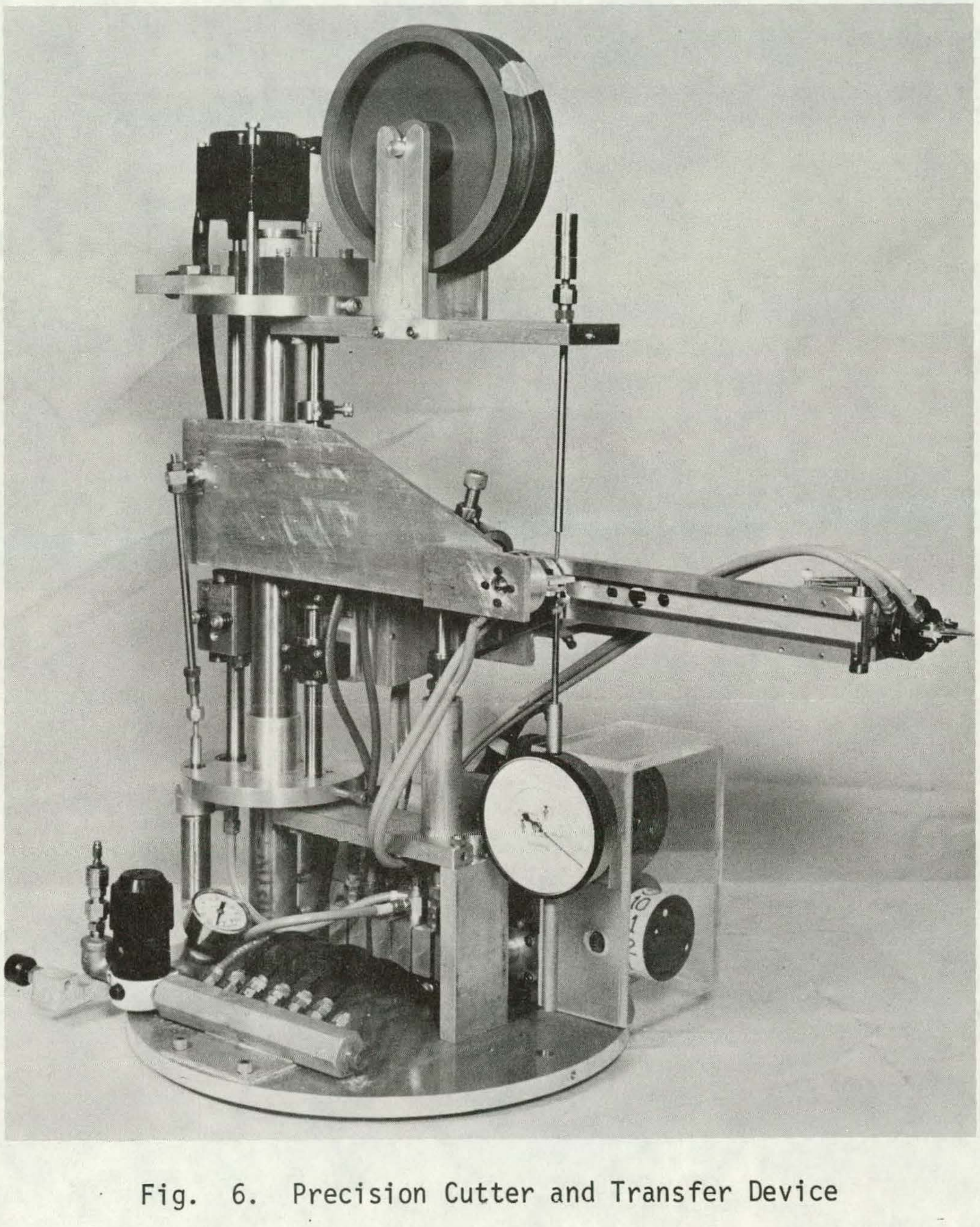


Fig. 6. Precision Cutter and Transfer Device

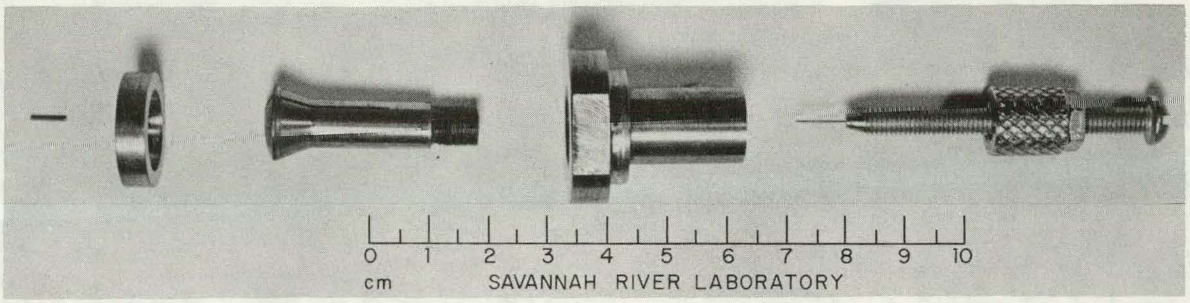


Fig. 7. Disassembled View of Collet for Handling ^{252}Cf Seed Capsules

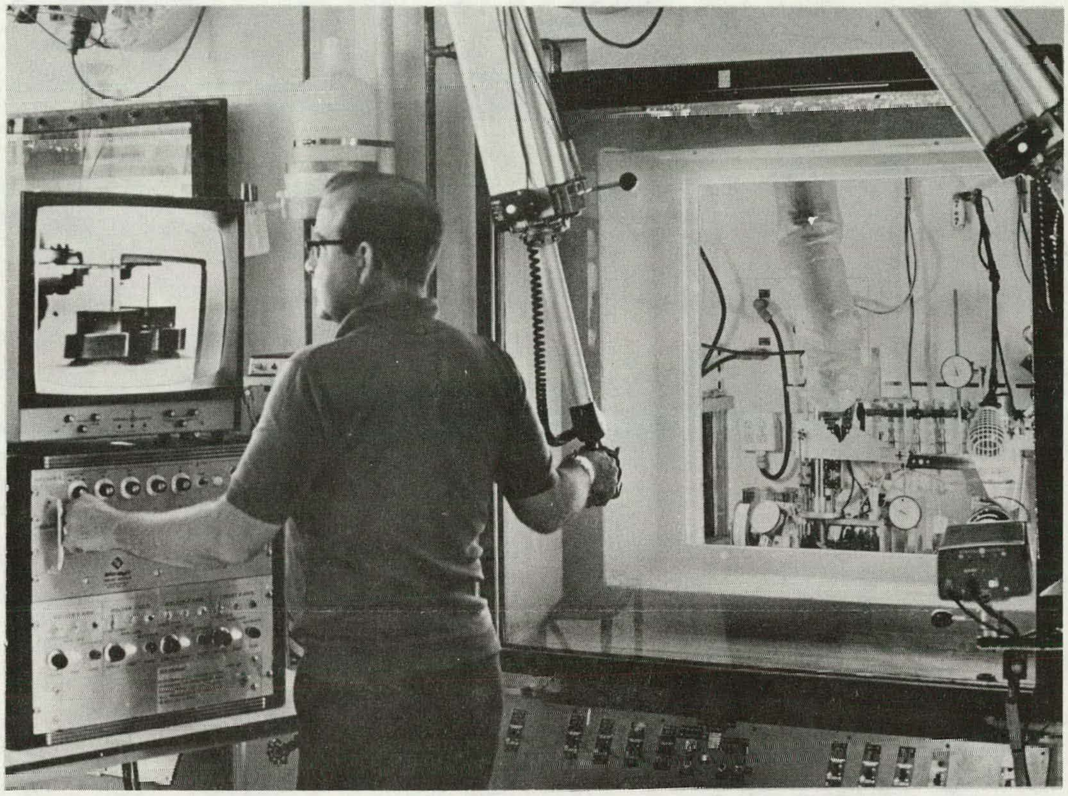


Fig. 8. Operator Inserting Wire in Capsule on XYZ Stage. Video Camera at Lower Right is Observing Operation Through Cell Window

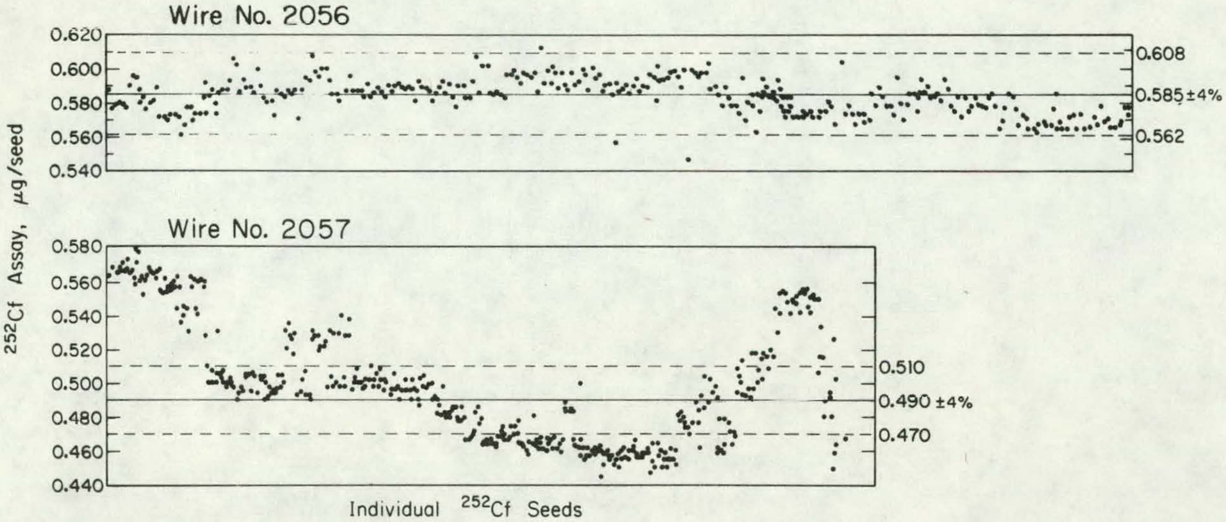


Fig. 9. ^{252}Cf Assay Control Chart

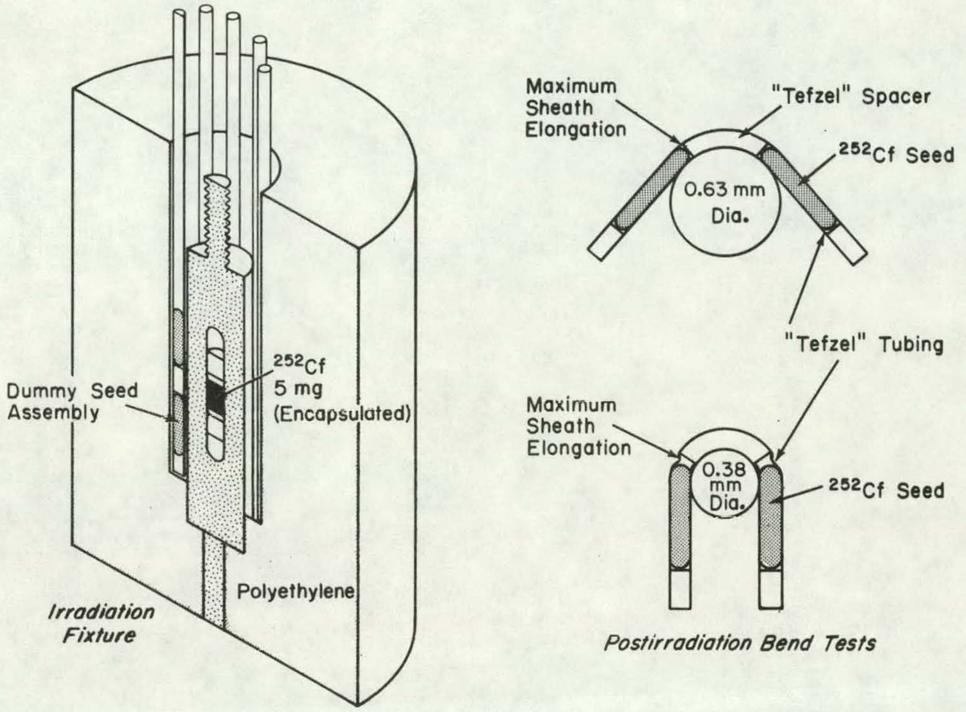


Fig. 10. Irradiation Test of "Tefzel" Components

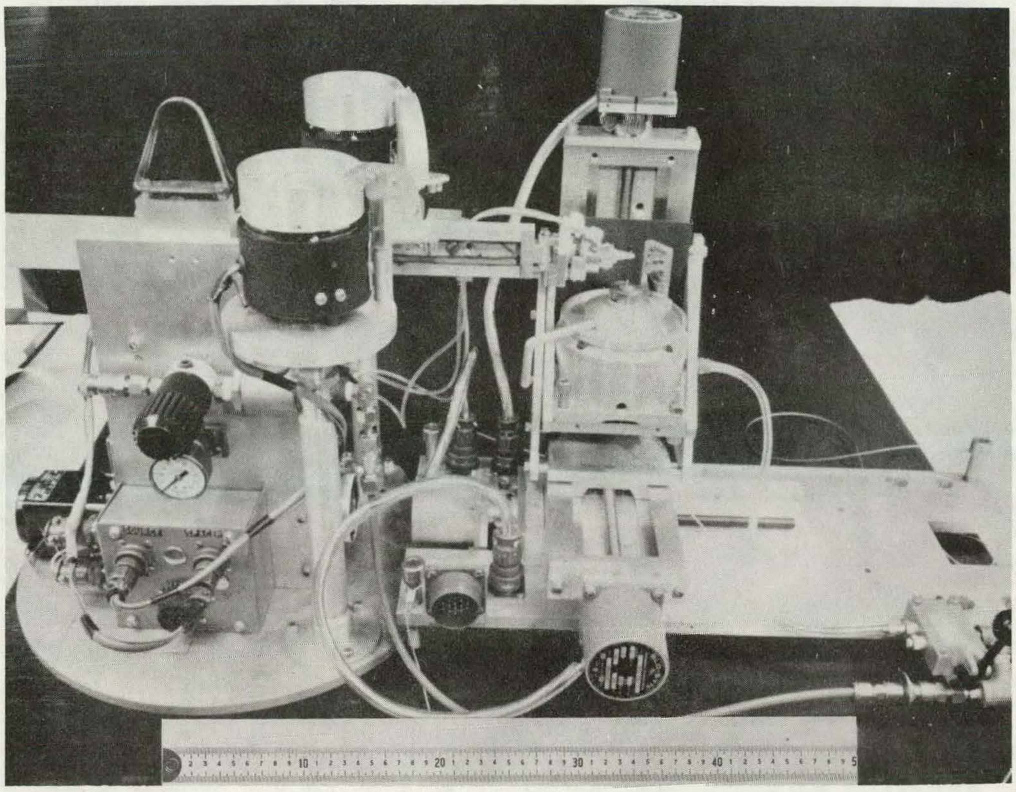


Fig. 11. Stacking and Transfer Machine Operation With Positioner

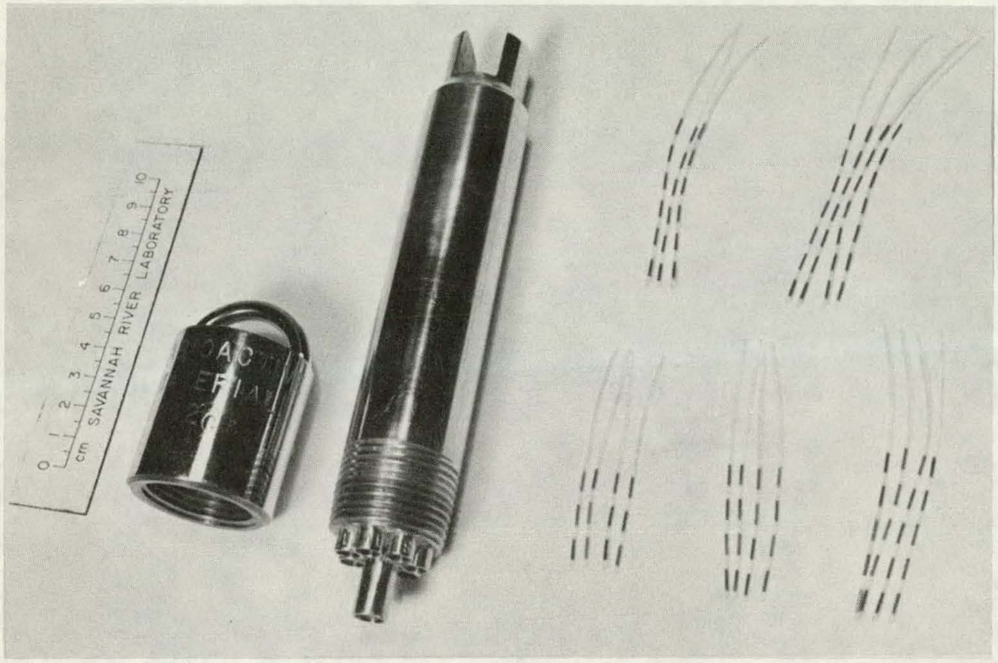


Fig. 12. Shipping Cartridge and Standard Inventory of ^{252}Cf Seed Assemblies