DOSE DISTRIBUTION OF MODEL 6712 ^{125}I SOURCES

A Report Submitted to the
Radiation Products Division
3M Company
St. Paul, Minn.

by

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ABSTRACT

Dose distributions in water of a new I-125 seed, Model 6712, have been measured to a distance of 7 cm from the seed center. A silicon diode and electrometer were used in the measurement. At any given distance r from the seed center, the dose varies with θ, the angle relative to the seed axis. Similarly, the r dependence of the dose distribution is different at various θ values. Two empirical models have been fitted to the data.

INTRODUCTION

Encapsulated ^{125}I seeds are presently being used in intraoperative permanent interstitial implants of the prostate, apical lung, and pancreatic carcinomas, in permanent or temporary implants of glioblastoma multiforme, and, as plaques in ocular tumors.[1-5] Because of the low energy of ^{125}I photons and the associated ease in radiation shielding, its use as a substitute for Cs-127 and Ir-192 in temporary implants can be envisaged, providing the economic factors of the different modalities are comparable.

Recently a new type of encapsulated ^{125}I seed, model 6712, has been produced by the manufacturer.* The design goal was to make the seed smaller, to simulate the dimensions of Ir-192 sources. The basic configuration of a 6712 seed resembles that of a 6711 seed. A seed consists of ^{125}I absorbed on a silver wire and contained in an titanium tubing with both ends welded. The overall outer dimensions are 4.5 mm long X 0.5 mm in diameter for model 6712, and 4.5 mm long X 0.8 mm in diameter for model 6711 sources, respectively. This study was initiated to examine the physical characteristics of ^{125}I sources with the new encapsulation design. In particular, we measured the two-dimensional dose distribution for model 6712 ^{125}I seeds and used empirical mathematical expressions to represent the measured data. A similar study of the model 6711 seeds[6] and the model 6702 seeds[8] has been previously reported.

MATERIALS AND METHODS

Relative dose distributions in water about the model 6712 ^{125}I seeds were obtained with a silicon diode,[+] an electrometer,[++] and a Therados Radiation Field Analyzer (RFA-3).[+++] The small size (2.2 X 2.3 X 0.05 mm with 1 mm thick tissue equivalent plastic front covering) and high sensitivity of this solid state detector, with the precise positional control (better than $\pm$0.1 mm) of the RFA-3, make this system well suited for this measurement.

The two dominant interactions of ^{125}I photons in water are the photoelectric effect and the Compton scattering. In a photoelectric interaction, the ^{125}I photon is completely and locally absorbed. In contrast, only a small fraction of the incident photon energy is imparted to a recoil electron from Compton scatter. Also, the ratio of mass energy absorption coefficients of silicon to water varies by less than 5% for photons with energies between 15 kev and 35 kev. Therefore, the response of the diode is essentially proportional to the dose in water for all distances from the seed.[6,7]

The diode position relative to the ^{125}I seed was accurately controlled ($\pm$0.1 mm).[+++] The extremely thin intrinsic junction of the diode allows for fine resolution in one direction of the dose distribution. The photon interactions induced currents in the p-n junction of the diode ranging from nanoamperes to picoamperes, depend on the distance between the seed and the diode. A small but measurable background current was recorded and subtracted. The background current was less than 1% of the total current at small distances from the seed and approached about 11% of the total current at a distance (r) of 7 cm and an angle (θ) of 180°.

To measure the dose distribution data, the diode was positioned at various distances from a seed center. The seed was then rotated about its perpendicular bisector by using a precisely machined jig which held the seed in a water phantom. The readings, displayed on the digital electrometer[++] and recorded, were measured as a function of the angle relative to the seed axis. The data were then normalized to unity at a distance of 1 cm (seed center to diode junction) along a θ of 90°. Data were taken for 150°, 160°, 170°, and 180° relative to the seed axis, and at corresponding angles in the other quadrants. Results obtained at angles symmetric relative to the seed axis were averaged. A high activity seed (45

mCi) was used in this measurement to provide a sufficiently high signal-to-noise ratio.

RESULTS

As previously described, data were taken with the diode at various distances from the seed center, and the seed was rotated about its perpendicular bisector. 0° and 180° were defined to be along the seed axis in opposite directions. The relative dose as a function of distance from the seed center has been determined for the angles 90°, 150°, 160°, 170°, and 180° with respect to the seed axis. This data set, which is normalized to 100% at 1 cm along the seed's perpendicular bisector, is shown in Figure 1 as a relative dose rate distribution. The inverse square dependence has been removed from the data, by multiplying each data point by the square of the distance from the seed center, to better appreciate the effects of attenuation, independent of the inverse square effect.

The radial dependence of the relative dose rate distribution varies with angle (θ) about the seed axis such that the dose is significantly reduced along the seed axis (0° or 180°), relative to that along the perpendicular bisector. At 90°, the relative dose rate distribution decreases monotonically with distance from the seed center. At 180°, however, the relative dose rate distribution exhibits a more rapid decrease between 0.5 and 1.5 cm, and a slower drop off between 1.5 and 3.5 cm. The dose rate values for intermediate angles vary gradually between these two extremes. The $\pm$0.1 mm precision of the measurement system accounts for the uncertainty of the data at small distances from the seed. At large distance, the uncertainty stems primarily from noise.

Two mathematical formulae, used earlier for the data of model 6711[6] and model 6702[8] seeds, are used to represent the measured data. In the first method, the dose pattern is described by the product of two polynomials and an exponential term (the double polynomial model):

$$D(r,\theta) \cdot r^2 = \exp(-\mu r) \cdot (A + Br + Cr^2) \cdot (1 + a\theta + b\theta^2 + c\theta^3) \qquad (1)$$

In this representation, the product, $D \cdot r^2$, is described by the following: (1) an exponential term which describes the attenuation with distance from the seed center, (2) a quadratic polynomial which is r-dependent, and (3) a cubic polynomial which is θ-dependent. The parameters for the radial quadratic are determined by the data taken along the seed's perpendicular bisector. These parameters are then fixed and the angular distribution parameters are fit to entire data set. The procedure implies the same r dependence at all values of θ.

The second model (termed "the matrix fit") involves the product of an exponential attenuation term and a radial distribution polynomial, the parameters for which are θ-dependent:

$$D(r,\theta) \cdot r^2 = \exp[-\mu(\theta).r] \cdot [\alpha(\theta) + \beta(\theta)r + \gamma(\theta)r^2] \qquad (2)$$

The fit of Eqs. (1) and (2) to the measured data can be obtained with a nonlinear regression by the least squares method, as was performed previously for model 6711 and 6702 sources.[6,8] However, because of the similar design of the model 6711 and 6712 sources, and the similiarity in the measured dose distribution, we simply use the parameters previously used for model 6711 seeds.[6] Tables 1 and 2 list the best fit parameters, with distance in cm and angle in degrees, for the double polynomial fit and the matrix fit respectively. The comparison of the measured data and the mathematical representation is shown in Figures 1 and 2. The figures show good agreement between the measured and calculated results.

A polar coordinate plot of the relative dose rate distribution at fixed distances is shown in Fig. 3. It indicates that the dependence on θ gradually decreases as distance increases. For instance, the ratios of dose rate values at 180° and 90° are 0.39 at 1 cm and 0.48 at 5 cm, respectively. Thus, the anisotropy of the relative dose rate distribution decreases as r increases. This result reflects the effect of increased scatter with distance, smoothing out the variation in photon output caused by the differential absorption in the source capsule.

SUMMARY

The two-dimensional dose distribution in water about the new model 6712 ^{125}I seed has been experimentally determined. The measured data closely resemble those of model 6711 sources. In fact, the same parameters can be used in the two mathematical expressions to represent the measured results of both models of seeds, without sacrificing accuracy. These data can be incorporated into computerized dose distribution calculation to give accurate implant dosimetry when model 6712 is available in the clinic.

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* Obtained from Medical Products Division/3M, New Brighton, MN 55112.

\+ Manufactured by Therados of Uppsala, Sweden.

++ Model 616 electrometer by Keithley Instruments Inc. of Cleveland, Ohio.

+++ Radiation Field Analyzer (RFA-3) by Therados of Uppsala, Sweden.

TABLE 1. Best-fit values of the parameters using the double polynomial method (see text).

μ	0.48 (±0.02)
A	1.13 (±0.03)
B	0.48 (±0.04)
C	0.0081 (±0.0089)
a	−0.0046 (±0.0009)
b	9.7 (±1.4) × 10^{-5}
c	−4.99 (±0.01) × 10^{-7}

TABLE 2. Best-fit values of the parameters using the matrix fit method (see text).

θ	α	β	γ	μ
90°	1.13 ± 0.03	0.48 ± 0.04	0.008 ± 0.004	0.48 ± 0.02
150°	1.06 ± 0.03	0.30 ± 0.03	0.10 ± 0.05	0.58 ± 0.05
160°	0.87 ± 0.03	0.25 ± 0.03	0.15 ± 0.04	0.63 ± 0.03
170°	0.69 ± 0.06	0.054±0.099	0.21 ± 0.07	0.69 ± 0.05
180°	0.69 ± 0.04	−0.19 ± 0.08	0.33 ± 0.05	0.78 ± 0.03

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(4) Gutin, P.H. et al: Permanent and removable implants for the brachytherapy of brain tumors. Int. J. Radiat. Oncol. Biol. Phys. 7: 1371-1381, 1981.

(5) Packer, S. et al: Radiotherapy of choroidal melanoma with ^{125}I. Ophthalmology 87(6): 582-590, 1980

(6) Ling, C.C. et al: Physical dosimetry of ^{125}I seeds of a new design for interstitial implant. Int. J. Radiat. Oncol. Biol. Phys. 9: 1747-1752, 1983.

(7) Dale, R.G.: Some theoretical derivations relating to the tissue dosimetry of brachytherapy nuclides, with particular reference to ^{125}I. Med. Phys. 10: 176-183, 1983.

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Relative Dose At Various Distances Around I-125 Source

(Measured Data For Model 6712)

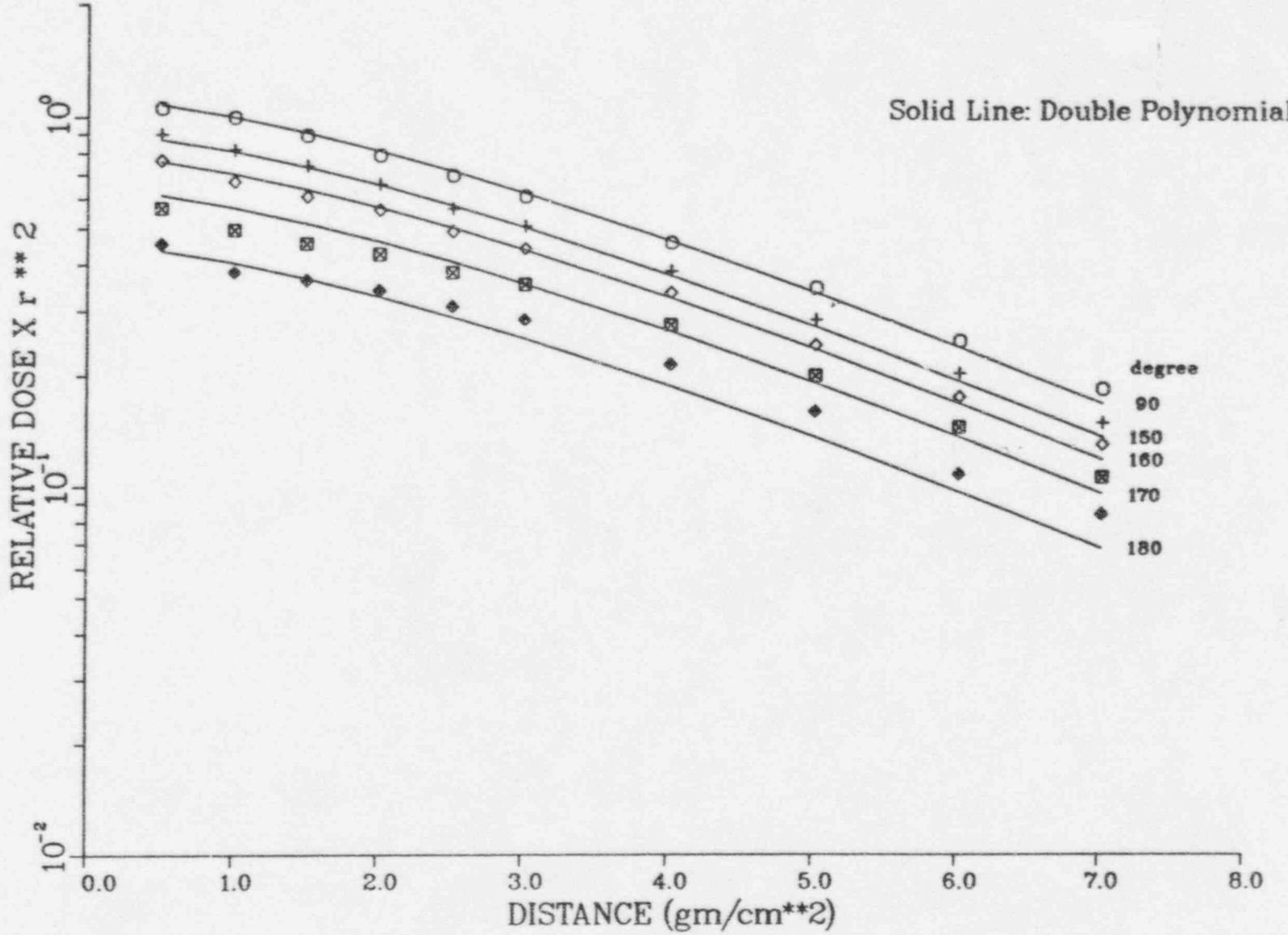


FIG. 1

Relative Dose At Various Distances Around I-125 Source

(Measured Data For Model 6712)

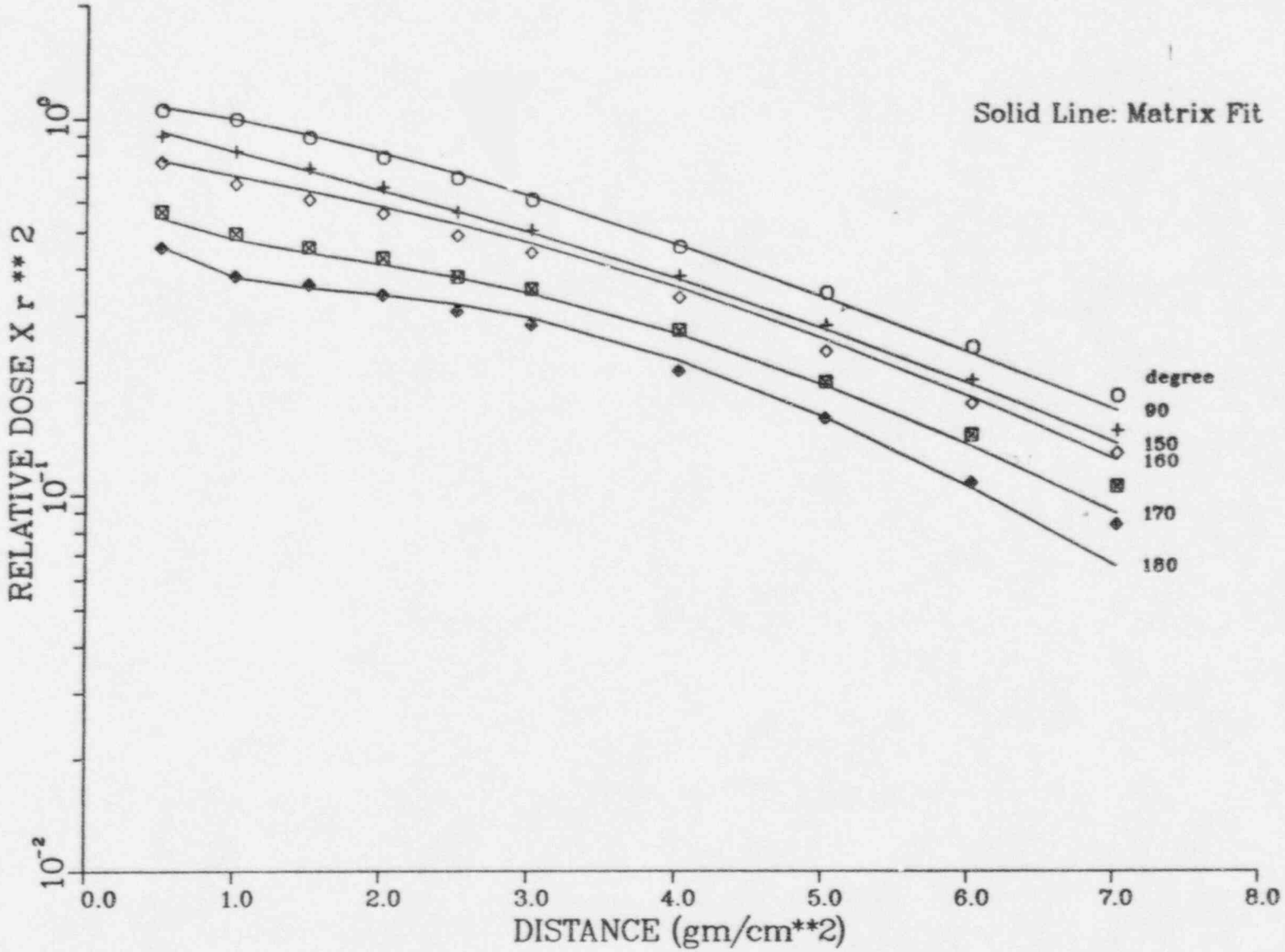


FIG. 2.

Relative Dose At Various Distances Around I-125 Source

(Measured Data For Model 6712)

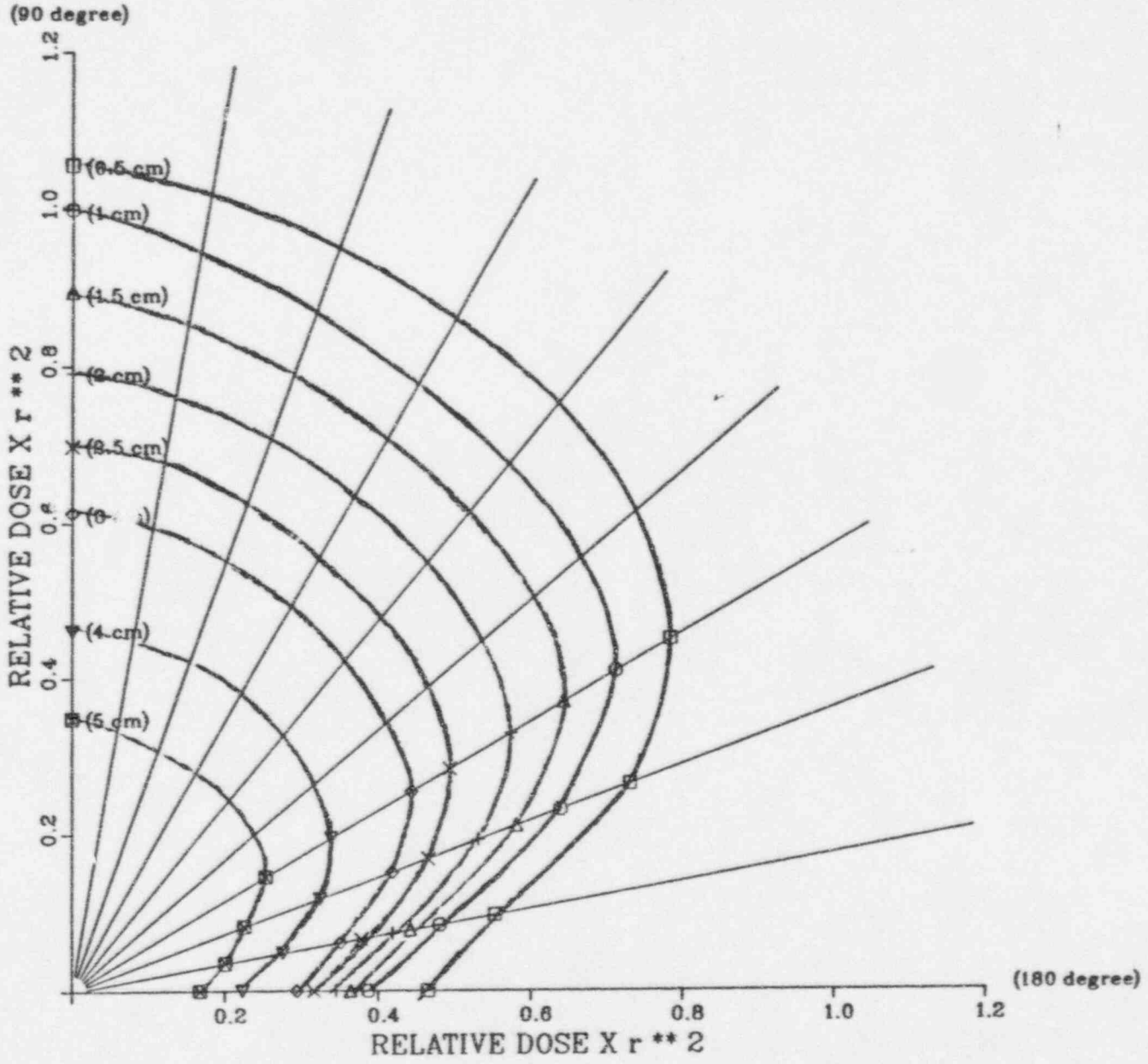
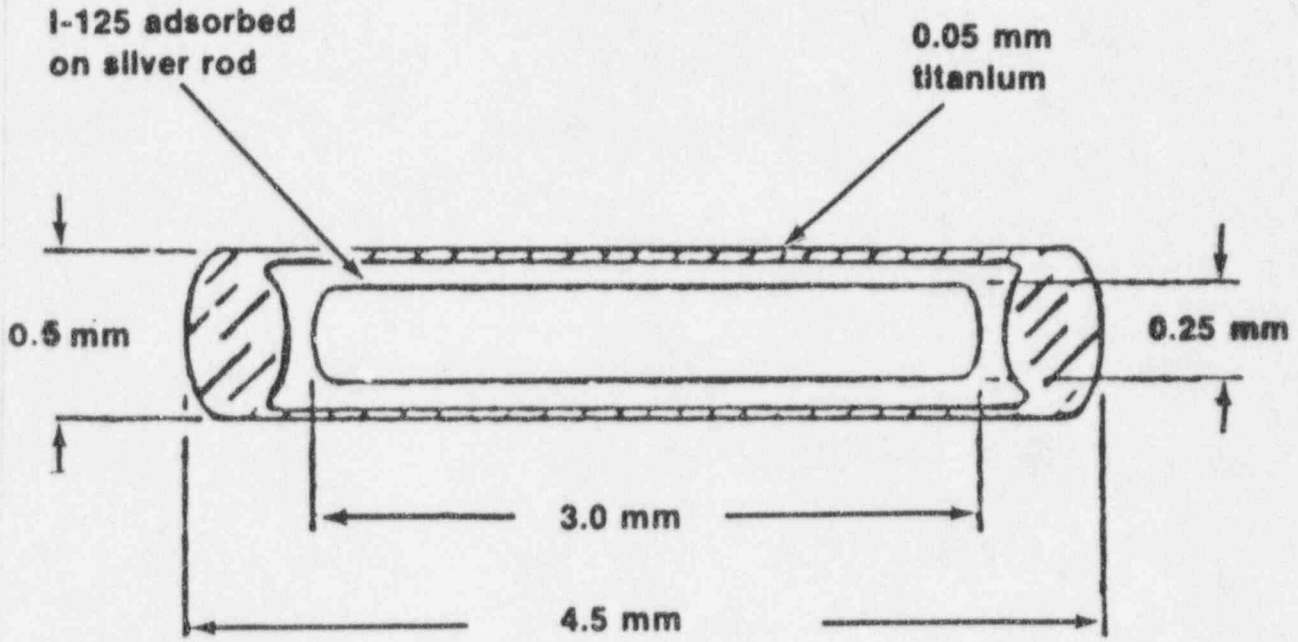


FIG. 3

MODEL 6712

I-125 SEED



ATTACHMENT C: Shear data for titanium tubing used in Model 6702, Model 6711 and Model 6712 I-125 Seeds.

In a report to you from J. Bush of 3M dated July 8, 1988 we showed the force in kilograms necessary to shear or cut lengths of titanium just behind the weld made using either tungsten inert gas (TIG) welding or a new plasma arc welding (PAW). The forces (shown below) were statistically the same for both welders:

Shear Results for Titanium Tubing used for Model 6702 and Model 6711 I-125 Seeds - July 88.

Weld Type	n	Shearing force (kg) +/- 1 SD
TIG	10	11.4 +/- 0.8 (7.0%)
PAW	10	12.0 +/- 0.8 (6.7%)
tubing only, no weld	2	6.5 +/- 0.4 (6.2%)

Recently, shear tests (shown below) were repeated on the titanium tubing used to manufacture the Model 6702 and Model 6711 I-125 Seeds and on the smaller diameter tubing to be used in the Model 6712 I-125 Seed, PAW welding - September 1989

Seed Type	n	Shearing force (kg) +/- 1 SD
Model 6702 & 6711 tube with weld	10	12.1 +/- 1.4 (11.6%)
Model 6702 & 6711 tubing only	10	13.3 +/- 0.5 (3.8%)
Model 6712 tube with weld	5	6.4 +/- 0.6 (9.4%)
Model 6712 tubing only	5	8.1 +/- 0.2 (2.5%)

RESULTS AND DISCUSSION

Model 6702 and Model 6711 I-125 Seed Tubing

Welded Tubing

The July 88 and September 89 shear results for the welded tubing used in the Model 6702 and Model 6711 I-125 Seeds agree quite well (12.0 kg vs. 12.1 kg).

Tubing only

Results for the tubing only, disagree. The July 88 shear force (6.5 kg) was 49% of the 13.3 kg shear force measured in September 89. We have concluded that better technique and more samples produced a more reliable result in the September 89 tests.

Welded tubing vs. tubing only

In the September 89 tests, the force required to cut the welded tubing just behind the weld was 12.1 kg or 91% of the 13.3 kg force required to cut the tubing only. As indicated by the standard deviation, the shearing force was also more variable for the welded tubing.

Model 6712 Tubing vs. Model 6702 & Model 6711 tubing

Welded Tubing

In the September 89 results, the force required to cut the Model 6712 welded tubing just behind the weld was 6.4 kg. This is 53% of the 12.1 kg force required to cut the welded tubing used in the Model 6702 and Model 6711 I-125 Seeds.

Tubing only

Comparing tubing alone (8.1 kg vs 13.3 kg), the tubing used in the Model 6712 I-125 Seed was cut with 61% of the force required to cut the tubing used in Model 6702 and Model 6711 Seeds.

Welded tubing vs. tubing only for the Model 6712 Seed

In the September 89 results, the force necessary to cut welded tubing just behind the weld was 6.4 kg or 79% of the 8.1 kg force required to cut the tubing alone. Results are also more variable for the welded tubing as indicated by the standard deviation.

Shear Force

True shear force is defined as force per cross-sectional area and not the absolute force required to cut the titanium tubing as presented here. Using this definition, both types of titanium tubing have similar shear because the cross sectional area of the smaller tubing intended to be used in the Model 6712 I-125 Seed is about 59% of that used in the Model's 6702 and 6711 I-125 Seeds.

SUMMARY AND CONCLUSIONS

The titanium tubing (with and without weld) intended for use in production of the Model 6712 I-125 Seed can be sheared or cut with 53% to 61% of the forces required for cutting titanium tubing (with and without weld) used to manufacture Model 6702 and 6711 I-125 Seeds. Both types of tubing have similar wall thicknesses of about 50 um, but the former has a cross sectional area 59% smaller than the latter. This accounts for the smaller absolute shear force but results in a similar force per unit cross sectional area.

Whether an absolute shearing force of 6.4-8.1 kg can be regarded as contributory to the production of "weaker" or more "hazardous" Model 6712 I-125 Seed is open to speculation. This is still a significant force (14.1-17.9 pounds) required to cut a Model 6712 Seed accidentally. Our warning (see attached) included in each I-125 Seed shipment has virtually eliminated such cut or damaged Model 6702 and 6711 I-125 Seeds and is expected to do so for the Model 6712 Seed.

Warning:

I-125 SEEDS INTENDED FOR PERMANENT IMPLANT

Do not force an I-125 Seed into (or from) any implant tube, needle, or cartridge; doing so may damage the wall or end welds of the Seed potentially causing release of I-125 into the environment and into body fluids should the Seed be implanted. If a Seed has been visibly damaged in any way, discard it immediately to radioactive waste and check the area for contamination. UNDER NO CIRCUMSTANCES SHOULD VISIBLY DAMAGED SEEDS BE IMPLANTED.

I-125 SEEDS INTENDED FOR TEMPORARY IMPLANT AND REUSE

When loading or removing I-125 Seeds from plastic or rubber afterloading catheters, use a vented chemical hood which has adequate air flow up the stack and a filtered exhaust. If a chemical hood is not available, a plastic glove box specifically designed for work with radioactive iodine may be substituted, provided it is properly vented.

If a razor blade, scalpel, or other sharp tool is used to remove I-125 Seeds from the afterloading catheters, use extra care to avoid contacting or cutting a Seed. A Seed which has been damaged (nick, cut, slice, or other type of damage) will release I-125 into the environment.

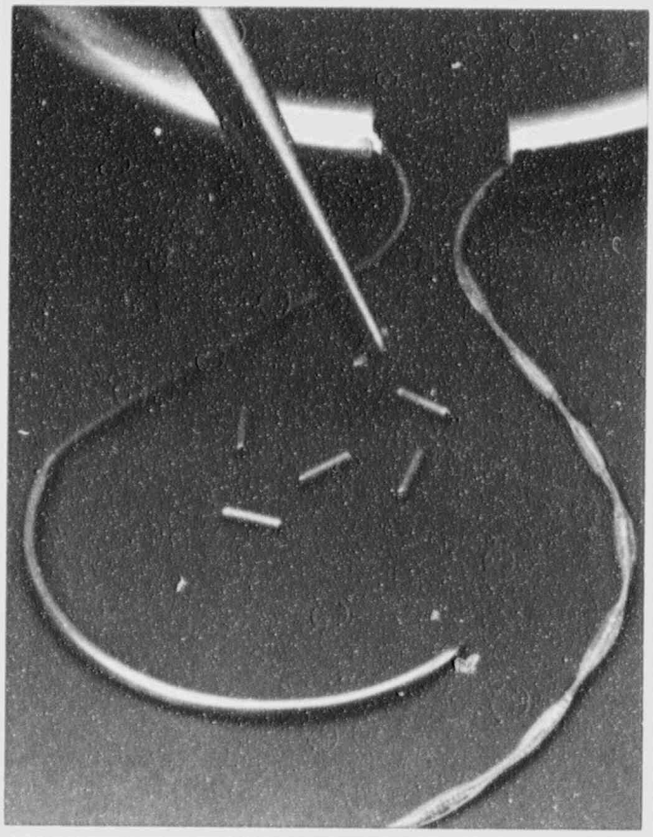
To assure that Seeds have not been damaged following removal from the afterloading catheters, conduct a contamination survey with a radiation monitor capable of detecting 30 keV photons. This survey should include wipe (or leak) tests of Seeds and an overall area survey. For Seed leak test details, contact 3M Customer Service at 1-800-328-1671. Residents of Minnesota or Canada call 612-733-9181.

34-7023-4606-4

FOR REFERENCE

I-125 Seeds®

for Interstitial Radiation Therapy



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3M
HealthCare

General Information

Development

Use of iodine-125 in seeds originated at Memorial Sloan-Kettering Cancer Center where the first implant took place in 1965. Memorial recognized the need for a low-energy brachytherapy source, the use of which would result in reduced radiation exposure to medical personnel, patients and their families (1,2).

I-125 Seeds® became commercially available in 1968 from Lawrence Soft Ray (LSR) of Sunnyvale, California (3) and in 1978 from 3M following acquisition of LSR. A year later, 3M moved I-125 Seed production from Sunnyvale to New Brighton, Minnesota, a suburb north of St. Paul.

3M continued to manufacture LSR's line of low-activity (less than 1 mCi) Model 6701 I-125 Seeds containing a gold X-ray marker and high activity (1 to 40 mCi) Model 6702 I-125 Seeds containing no X-ray marker. In 1983, 3M replaced Model 6701 I-125 Seeds with Model 6711 I-125 Seeds having improved X-ray visibility. In the same year, 3M began assaying all production I-125 Seeds against I-125 Seeds calibrated by the National Bureau of Standards.

Iodine-125 Seeds in absorbable suture was anticipated (4), introduced (5,6) and developed (6,7) in 1974-75. This product is useful for shallow plane implants of I-125 Seeds where standard I-125 Seed implanters are less suitable. Lawrence Soft Ray manufactured I-125 Seeds in Vicryl® suture during the years 1975-76. 3M re-introduced the product in 1982 as Model 6720 I-125 Seeds in Carrier.

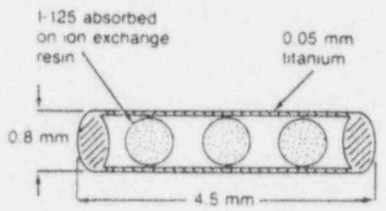
Description

I-125 Seeds

Iodine-125 Seeds range from 4.2 mm to 4.9 mm in length and from 0.77 to 0.96 mm in diameter. The shell material is titanium tubing having a wall thickness of 0.05 mm with welds at both ends. Depending on design, the I-125 Seed contains the following:

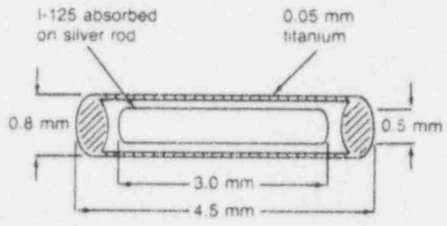
Model 6702 — Two to five resin spheres with absorbed iodine-125 (3).

Model 6702

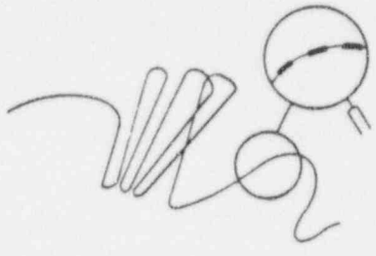


Model 6711 — One silver rod serving both as an x-ray marker and a carrier for iodine-125 (8).

Model 6711



Model 6720



I-125 Seeds in Carrier

Model 6720 — I-125 Seeds in Carrier consists of Model No. 6711 I-125 Seeds spaced at a fixed distance within #1 Vicryl (polyglactin 910) absorbable suture. The portion of the suture containing the I-125 Seeds is housed in a stainless steel ring (9) which attenuates >99.9% of the I-125 photons. I-125 Seeds in Carrier is sterile when shipped.

How Supplied

I-125 Seeds

Model No. 6702 I-125 Seeds are available with apparent activities from 5.0 to 40 mCi per I-125 Seed.

Model No. 6711 I-125 Seeds are available with apparent activities from 0.10 to 4.9 mCi per I-125 Seed and, by special request, from 5.0 to 40 mCi per I-125 Seed.

Model 6702 and **6711** I-125 Seeds are packaged in a shrink-wrapped screw-cap glass vial, which is labeled with: activity range in mCi; total activity in mCi; assay date; number of I-125 Seeds and I-125 Seed lot number. The glass vial is contained in a shrink-wrapped lead "pig" similarly labeled. The pig label has, in addition, precautionary regulatory statements pertaining to licensing of the I-125 Seeds.

I-125 Seeds are NOT sterile when shipped.

I-125 Seeds in Carrier

Model 6720 I-125 Seeds in Carrier is STERILE having ten I-125 Seeds spaced 1 cm center to center in a braided #1 Vicryl (polyglactin 910) suture. The usual activity range for the ten I-125 Seeds is 0.40 to 0.42 mCi. Other activity ranges may be available. These vary from 0.2 to 1.0 mCi, each having a 6% activity spread. Other configurations of I-125 Seeds in Carrier (up to 20 I-125 Seeds with I-125 Seed spacing ranging from 0.5 to 1.5 cm center to center) may be available at special request.

A ½ circle taper point needle is attached to one end of the suture. The distal end of the suture containing the I-125 Seeds is housed within a stainless steel ring.

The stainless steel ring is sealed in a moisture-resistant foil bag which is enclosed in a Steri-Lok® gas sterilization bag.

Affixed to the Steri-Lok bag are two labels showing the following information: 1) activity range in mCi; total activity; number of I-125 Seeds; assay date; I-125 Seed lot number and I-125 Seed spacing and 2) "Sterility guaranteed unless package is damaged or open".

The Steri-Lok bag is enclosed within a clear plastic bag which must remain intact in order for the I-125 Seeds in Carrier to be returned for partial credit.

Directions For Use

Indications

Permanent implants of low-activity I-125 Seeds (strengths of less than 1 mCi) are indicated for interstitial treatment of tumors which are either unresectable or residual after excision of the primary lesion; localized; of slow growth rate; and which have low to moderate radiosensitivity (10).

Temporary implants of high activity I-125 Seeds (strengths greater than 1 mCi) are indicated for treatment of tumors which are either unresectable or residual after excision of the primary lesion; localized; and which have moderate radiosensitivity (10).

Use of I-125 Seeds may be indicated for use concurrent with or at the completion of other treatment modalities, such as external beam therapy, hyperthermia or chemotherapy (10).

I-125 Seeds have been used primarily as permanent implants in tumors of the prostate, lung, head and neck and pancreas, and as temporary implants in tumors of the breast (11,12), brain and eye (13).

I-125 Seed Implant Activity and Nomogram

A simple empirical formula has been developed by Memorial Sloan-Kettering Cancer Center (MSKCC) to calculate the activity required to treat a given tumor volume. In this "dimension averaging" technique, total millicuries of iodine-125 implanted is determined by multiplying the average of the three mutually perpendicular implant dimensions by an appropriate factor (1).

This formula has undergone change at MSKCC over the years (1,14,15). The formula used by MSKCC since 1984 is the following (15):

For the implant with an average dimension d(a), the iodine-125 activity implanted is calculated as follows:

Average dimension d(a)	Implanted Activity	Tumor dose
<3.0 cm	5 x d(a)	480 Gy /d(a)
>3.0 cm	1.34 x $d(a)^{2.2}$	160 Gy

Where average implant dimension d(a) = (a + b + c)/3

An implant nomogram is available from MSKCC which incorporates the above formula so that "recommended (implant) activity" can be read directly from a scale next to an "average dimension" scale. The nomograph also gives the number of I-125 Seeds of a given activity required, and the spacing to be used between needles for a given spacing of Seeds along the needle.

Memorial Sloan-Kettering Cancer Center cautions that, whereas this nomogram represents current practice there, each institution using I-125 Seeds must decide its own treatment policy.

Implant Devices

Permanent implants — I-125 Seeds are implanted using an I-125 Seed "applicator" attached to a 17 gauge or larger needle. Common Seed applicators are the Mick, Henschke and Scott. The Royal Marsden Gold Grain gun can be used to implant Seeds provided a special modification is requested of the manufacturer. Model 6720 I-125 Seeds in Carrier needs no additional applicator.

Temporary implants — I-125 Seeds are usually loaded into plastic tubing or other devices (e.g. gold eye plaques) to facilitate afterloading procedures and I-125 Seed recovery.

Dosimetry

Dose distribution around I-125 Seeds is not isotropic. This anisotrophy should be included in dose distribution calculations (16, 17, 18, 19).

Physical Properties

Table 1 shows physical characteristics of iodine-125 compared with other radionuclides used for interstitial implants. The chief advantage of iodine-125 (and newcomer palladium-103) is ease of shielding, which results in reduced exposure to attending personnel, patients and visitors (1,2). Additionally, the titanium encapsulation of I-125 Seeds (and palladium seeds) insures good tissue compatibility and minimal self-absorption of the low-energy photons (20).

Table 1. Radionuclides for Interstitial Implants (21).

Isotope	Half Life (days)	Emitted Beta (max)	Energy (keV) Gamma	Half Value Layer (lead)	Half Value Layer (tissue)
gold-198	2.7	960	412	2.6 mm	6 cm
palladium-103	17.0	none	20-23	0.008 mm	1 cm
iodine-125	59.6	none	27-35	0.025 mm	2 cm
iridium-192	73.8	672	296-612	2.6 mm	6 cm

Iodine-125 has a half-life of 59.6 days (21) and decays by electron capture with the emission of characteristic photons and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal photon emissions are 27.4 and 31.4 keV x-rays and a 35.5 keV gamma. Also emitted from Model 6711 Seeds are 22.1 and 25.2 keV fluorescent x-rays from the silver rod (22). Table 2 shows the decay of iodine-125.

Table 2. Iodine -125 Decay Table

Days	Decay Factor	Days	Decay Factor
0	1.000	36	0.658
2	0.977	38	0.643
4	0.955	40	0.628
6	0.933	42	0.614
8	0.911	44	0.599
10	0.890	46	0.586
12	0.870	48	0.572
14	0.850	50	0.559
16	0.830	52	0.546
18	0.811	54	0.534
20	0.792	56	0.521
22	0.774	58	0.509
24	0.756	60	0.498
26	0.739	62	0.486
28	0.722	64	0.475
30	0.705	66	0.464
32	0.689	68	0.453
34	0.673	70	0.443

Radiation Protection

The 27-35 keV photons of iodine-125 are substantially absorbed by any high Z material but exhibit desirable penetration in tissue.

HVL Lead = 0.025 mm
HVL Gold = 0.01 mm
HVL Tissue = 20.0 mm

A thin lead sheet of only 0.25 mm (0.01 in) provides a 99.9% reduction in exposure.

Quality Assurance

Inspection

Each I-125 Seed is visually inspected, gauged for proper length and diameter, cleaned and leak tested, assayed (and assigned to an assay range) prior to shipment.

Leak Testing

I-125 Seeds are leak tested prior to shipment and have passed a leak test showing <0.005 uCi of removable iodine-125 as required by NRC regulation 10 CFR 35.59. This leak test value is printed on the Certification form that accompanies each shipment.

I-125 Seeds that retain clinical utility for more than six months must be leak tested "...at intervals not to exceed six months or at other intervals approved by the Commission or an Agreement State...(except for) sources stored and not being used. The licensee shall, however, test each such source for leakage before any use or transfer unless it has been leakage-tested within six months before the date of use or transfer..." as prescribed in 10 CFR 35.59.

I-125 Seeds intended for temporary implants (1 to 40 mCi) might fall into the above category and, if so, would need to be leak tested. Additionally, since the higher activity I-125 Seeds are often reused, leak testing at more frequent intervals is recommended. For leak test details, contact 3M Customer Service at 1-800-328-1671. Residents of Minnesota or Canada can call 612-733-9181.

Unused I-125 Seeds intended for permanent implants (nominal strength of 0.55 mCi) will not require additional leak testing providing they are disposed of within six months of the date shown on the I-125 Seed Certification form.

Calibration

Each production I-125 Seed is measured by comparison in a fixed geometry with an I-125 Seed of the same Model which has been calibrated by the U.S. National Bureau of Standards (NBS). For this comparison we use a Capintec Radioisotope Calibrator Model CRC-7R having a well re-entrant ionization chamber.

According to recommendations in AAPM Report No. 21(23), I-125 Seed standards calibrated by the NBS are specified in air kerma strength which is the product of air kerma rate and the square of the distance in vacuum in a direction perpendicular to the long axis of the I-125 Seed. The NBS reports air kerma strength of I-125 Seed standards in units of micrograys meters squared per hour ($uGym^2h^{-1}$) with an overall uncertainty of about +/- 5% (19).

Prior to using the NBS I-125 Seeds for calibration, we convert the stated air kerma strength into "apparent activity" in mCi (see Note) using an exposure rate constant of 1.45 R $cm^2h^{-1}mCi^{-1}$ (24) and the relationship that an exposure rate of 1 R/h is equivalent to an air kerma rate of 0.876 cGy/h (23). Apparent activity is a measure of output and not contained activity.

Following calibration, each low activity Model No. 6711 I-125 Seed is assigned to one of several mCi activity ranges having a total spread from 6-7% as shown in Table 3.

Table 3. Activity Ranges For Low Activity Model No. 6711 I-125 Seeds.

Millicuries	Air Kerma Strength (μGy m^2h^{-1})
0.97-1.04	1.23-1.32
0.89-0.96	1.13-1.22
0.82-0.88	1.04-1.12
0.76-0.81	0.97-1.03
0.70-0.75	0.89-0.95
0.65-0.69	0.83-0.88
0.60-0.64	0.76-0.81
0.55-0.59	0.70-0.75
0.51-0.54	0.65-0.69
0.47-0.50	0.60-0.64
0.43-0.46	0.55-0.58
0.40-0.42	0.51-0.53
0.37-0.39	0.47-0.50
0.34-0.36	0.43-0.46
0.31-0.33	0.39-0.42
0.28-0.30	0.36-0.38

When ordering I-125 Seeds, refer to the lowest number in the range, e.g. "0.55's" for the 0.55 to 0.59 mCi range. Although we inventory all activity ranges, sometimes a shortage occurs in a desired range. If this happens, other ranges may be suitable by making a small change in pretreatment dosimetry planning.

Medium activity Model No. 6711 I-125 Seeds having a range from 1 to 4.9 mCi (1.27 to 6.22 uGy m^2h^{-1}) and high activity Model No. 6702 I-125 Seeds having a range from 5 to 40 mCi (6.35 to 50.8μGy m^2h^{-1}), are inventoried in various activity ranges. These range values can be obtained by request from 3M Customer Service.

Note: We will continue to inventory I-125 Seeds in familiar mCi ranges during the transition between mCi and air kerma strength. Certification forms accompanying each I-125 Seed shipment will contain both mCi and air kerma strength values.

Additional Information

Warnings

I-125 Seeds Intended for Permanent Implant
Do not force an I-125 Seed into (or from) any implant tube, needle, or cartridge; doing so may damage the wall or end welds of the I-125 Seed potentially causing release of iodine-125 into the environment and into body fluids should the I-125 Seed be implanted. If an I-125 Seed has been visibly damaged in any way, discard it immediately to radioactive waste and check the area for contamination. UNDER NO CIRCUMSTANCES SHOULD VISIBLY DAMAGED I-125 SEEDS BE IMPLANTED.

I-125 Seeds Intended for Temporary Implant and Reuse
When loading or removing I-125 Seeds from plastic or rubber afterloading catheters, use a vented chemical hood which has adequate air flow up the stack and a filtered exhaust. If a chemical hood is not available, a plastic glove box specifically designed for work with radioactive iodine may be substituted provided it is properly vented.

If a razor blade, scalpel, or other sharp tool is used to remove I-125 Seeds from the afterloading catheters, use extra care to avoid contacting or cutting an I-125 Seed. An I-125 Seed which has been damaged (nick, cut, slice, or other type of damage) will release iodine-125 into the environment.

To assure that I-125 Seeds have not been damaged following removal from the afterloading catheters, a contamination survey should be conducted using a radiation monitor capable of detecting 30 keV photons. This survey should include wipe (or leak) tests of I-125 Seeds and an overall area survey. For I-125 Seed leak test details, contact 3M Customer Service at 1-800-328-1671. Residents of Minnesota or Canada call 612-733-9181.

Seed Sterilization

I-125 Seeds
I-125 Seeds are NOT sterile when shipped. Before implantation, they must be sterilized using steam or ethylene oxide (EO). DO NOT USE DRY HEAT OR CHEMICAL STERILIZATION.

Steam Sterilization (autoclave): Use the normal cycle (121 degrees C at 15 psi for 15 to 30 minutes) or the flash cycle (133 degrees C at 30 psi for about 3 minutes). DO NOT EXPOSE SEEDS TO TEMPERATURES AND PRESSURES IN EXCESS OF 138 DEGREES C and 35 PSI.

Ethylene Oxide (EO) Sterilization: Use cycle and aeration times recommended by the sterilizer's manufacturer or use those determined at the hospital.

Whether steam or ethylene oxide is used, I-125 Seeds should be sterilized in an adequately shielded container.

Lead Shipping Container: If I-125 Seeds are sterilized in the lead shipping container, the lead cover on the container and plastic cap on the glass vial therein should be removed to allow steam or ethylene oxide to access the I-125 Seeds.

Other Containers: I-125 Seeds can be loaded into stainless steel cartridges designed to be used with the Mick Applicator, or into the nylon and teflon tubes used with Henschke and Scott applicators. USE ETHYLENE OXIDE TO STERILIZE SEEDS LOADED INTO THE PLASTIC TUBES AS STEAM HEAT WILL WARP THE TUBES AND PREVENT SEED RECOVERY.

When in doubt about compatibility of steam heat with various I-125 Seed containers, load them with non-radioactive I-125 Seeds to determine the effect of steam on the container material and on I-125 Seed recovery.

I-125 Seeds in Carrier
This product is shipped sterile. DO NOT RESTERILIZE.

I-125 Seed Storage and Disposal

Iodine-125 is an accountable radioactive material. I-125 Seeds should, therefore, be strictly controlled and stored in a locked safe. If any significant material cannot be accounted for, the loss must be reported to the federal or state licensing agency.

For disposal, I-125 Seeds should be transferred to an authorized radioactive waste disposal agency. I-125 Seeds should never be disposed of in normal waste.

An I-125 Seed disposal service is provided by 3M Radiation Therapy Products. Customers wishing to use this service should contact 3M Customer Service for approval and specific information. In general, material approved for return must comply with Department of Transportation regulations (49 CFR Parts 171-177) regarding packaging and labeling. Shipments are to be directed to: 3M Radiation Therapy Products, TCAAP Building 590, New Brighton, MN 55112.

Licensing

The U.S. Nuclear Regulatory Commission has approved this sealed source (I-125 Seeds) for distribution to persons licensed to use byproduct material identified in paragraph 35.400 of 10 CFR Part 35, to persons who hold an equivalent license issued by an Agreement State and outside the United States to persons authorized by the appropriate authority.

Federal law restricts this device to sale by or on the order of a physician.

Specifications

Model No. 6702 and 6711 I-125 Seeds

	Model 6702	Model 6711
Dimensions	4.5 mm long, .8 mm OD .05 mm wall	4.5 mm long, .8 mm OD .05 mm wall
Encapsulation	titanium	titanium
Carrier for I-125	3-5 resin balls 0.6 mm diamter	silver rod 3 mm x 0.5 mm diameter
X-ray Marker	none	silver rod
Photon Energies	27.4 & 31.4 keV X-rays and a 35.5 keV gamma photon	Those of Model 6702 plus 22.1 & 25.2 keV fluorescent X-rays from the silver rod
Assay Method	CRC 7-R well re-entrant chamber calibrated using an I-125 Seed standard of the same Model which is traceable to the NBS	
Exposure rate constant	1.45 R cm^2 h^{-1} mCi^{-1}	1.45 R cm^2 h^{-1} mCi^{-1}
Seed Strength Specification	Apparent activity in mCi and air kerma strength. Both are descriptive of output and not contained activity.	
Available Seed Strengths	5.0 to 40 mCi 6.4 to 50.8 uGy m^2 h^{-1}	0.1 to 4.9 mCi 0.13 to 6.2 uGy m^2 h^{-1}

Model No. 6720 I-125 Seed in Carrier

#1 Vicryl (polyglactin 910) suture has an overall length of 78 cm and a half-circle taper point needle on one end. Model 6711 I-125 Seeds are located in the distal 15 cm of suture which includes a 5 cm tail.

I-125 Seed Count, Strength and Spacing:
Usually provided are ten I-125 Seeds having an activity range from 0.40 to 0.42 mCi which are spaced 1 cm center to center. Subject to availability are other loadings up to 20 I-125 Seeds; other activity ranges from 0.2 to 1.0 mCi (with a 6% activity spread in each range) and other spacings from 0.5 to 1.5 mm center to center.

Stainless Steel Ring:
Diameter is 84 to 86 mm. Diameter of cross section is at least 4.8 mm. Wall thickness is at least 1.7 mm. Attenuation of 30 keV photons is >99.9%. Surface dose rate with the usual I-125 Seed loading is <0.2 mR /h.

Packaging (exterior to interior):
Plastic dust cover; Steri-Lok bag; foil bag; folded white cardboard; stainless steel ring; I-125 Seeds in Vicryl suture.

Sterilization: Ethylene oxide.

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Steve, should I call 3M and get missing letters for

Missing the following letters:

July 8, 1988, 3 with enclosures thereto.

~~July 27, 1988~~

Brenda doesn't seem to have them.

Folder does not contain letters

NR-460-5-167-5

Do you have these letters? (NO)

MEMORANDUM OF CALL Previous editions usable

TO: TR

☑ YOU WERE CALLED BY– ☐ YOU WERE VISITED BY–

David

OF (Organization)

3M

☑ PLEASE PHONE ▶ ☐ FTS ☐ AUTOVON

612-733-9127

☐ WILL CALL AGAIN ☐ IS WAITING TO SEE YOU

☑ RETURNED YOUR CALL ☐ WISHES AN APPOINTMENT

MESSAGE

RECEIVED BY	DATE	TIME
	6/28	10:38

0 NSN 7540-00-634-4018 **STANDARD FORM 63** (Rev. 8-81)
Prescribed by GSA
FPMR (41 CFR) 101–11.6

1986 O - 157-353

MEMORANDUM OF CALL Previous editions usable

TO: ~~Bag~~ / Rich

☒ YOU WERE CALLED BY– ☐ YOU WERE VISITED BY–

David Kubiatowicz

OF (Organization)

3M

☒ PLEASE PHONE ▶ ☐ FTS ☐ AUTOVON

(612) 733-9127

☐ WILL CALL AGAIN ☐ IS WAITING TO SEE YOU

☐ RETURNED YOUR CALL ☐ WISHES AN APPOINTMENT

MESSAGE

status of model 6712
I-125 source.
leave message if machine
please
called 4:24 6/25/90 bmw

RECEIVED BY	DATE	TIME
MJ	6/25	3:30

63-110 NSN 7540-00-634-4018 **STANDARD FORM 63** (Rev. 8-81)
Prescribed by GSA
FPMR (41 CFR) 101–11.6

GPO : 1986 O - 157-353

April 1990

Medi-Physics
Mike Langton Rad

called David Kubatowicz
(612) 737-9127

6/28/90 9:01
left message on recording
called back 11:01 6/28/90

~~gave Perfluorocarbons over the phone~~

~~Need to Spell out Conditions of Use~~

- Need to Spell out Conditions of Use
- labeling
- ~~Engineering Analysis~~
- QA/QC

Warn about seeds being fragile

called 7/3/90 10:18
he called back 10:34 7/3/90

CONVERSATION RECORD

TIME: 2 3:30 | DATE: 7/31/91

TYPE: ☐ VISIT ☐ CONFERENCE ☒ TELEPHONE ☐ INCOMING ☐ OUTGOING

Location of Visit/Conference:

NAME OF PERSON(S) CONTACTED OR IN CONTACT WITH YOU	ORGANIZATION (Office, dept., bureau, etc.)	TELEPHONE NO.
David Kubiatowicz	3M	(612) 733-9127

ROUTING

NAME/SYMBOL	INT

SUBJECT

6712 I-125 SSD review

SUMMARY

I call David to find out status of telephone deficiency (called 6/28/90); He apologized for not getting back to me sooner. I was informed that Medi-Physics is going to manufacture this source at a later date. Therefore, action was closed out 7/31/91. A contact from Medi-Physics (Amersham owned?) will call at a later date and inform us on what they want to do with the sealed source application

ACTION REQUIRED

Close-out SSD

NAME OF PERSON DOCUMENTING CONVERSATION	SIGNATURE	DATE
Thomas W. Rich	Thomas W. Rich	7/31/91

ACTION TAKEN

SIGNATURE	TITLE	DATE

Medical-Surgical Division/3M

3M Center
St. Paul, Minnesota 55144-1000
612/733 1110

Rec'd 7/18

July 8, 1988

3M

Steven L. Baggett, Ph.D.
Health Physicist
U. S. NUCLEAR REGULATORY COMMISSION
Division of Fuel Cycle & Material Safety
MS-6-H-3
Washington, DC 20555

RE: I-125 Seeds 6702, 6711
Materials License No. 22-00057-59MD

Dear Dr. Baggett:

This letter is a follow-up to NRC's recent inspection of the New Brighton manufacturing facility and laboratory activities related to sources distributed by 3M under license 22-00057-59MD. Specifically, this letter addresses a violation identified by NRC during its exit interview of June 17th, pertaining to our need to submit to NRC information in support of a processing change for I-125 Seeds 6702 and 6711, with a request that the Certificates of Registration be revised accordingly.

Enclosed with this letter is a document entitled 'I-125 Seeds[R] 6702, 6711 - Justification for Manufacturing Change - Welding'. This document describes a change in the manufacture for I-125 Seeds from tungsten-inert gas (TIG) welding to a plasma arc-welding process, and presents data which indicate that Seeds produced by the plasma arc method are comparable to those produced by the TIG process and suitable for their stated intended use.

We trust that this information satisfies the agency's concerns about the integrity of the modified Seeds and is sufficient to support revision of the appropriate Certificates of Registration. If you have any questions, please feel free to call me (612/-733-6421).

Sincerely yours,

Jacquelyn D. Bush

JACQUELYN D. BUSH
Sr. Regulatory Affairs Specialist
3M Medical-Surgical Division
3M Center, Building 270-4A-05
Saint Paul, MN 55144-1000

JDB/llm
enclosure

1 SSpD

Log Aug. 88
Remitter
Check No. 328977 Dep. by RM
Amount $120
Fee Category 9C
Type of Fee AMD
Date Check Rec'd. 10/5/88
Date Completed 10/5/88
By: A. Hamilton

95+3080054 TPP

I-125 SEEDS® 6702, 6711

JUSTIFICATION FOR MANUFACTURING CHANGE -

WELDING

The following is submitted as justification for a revision in source certification documents for I-125 seeds 6702 and 6711, distributed under license 22-00057-59MD. Specifically, this information describes a change in the manufacturing process for these sources containing byproduct material and includes information to justify this change.

DESCRIPTION:

Each I-125 Seed® consists of a cylindrical titanium capsule containing I-125 absorbed onto either resin spheres (model 6702) or a silver rod (model 6711) and welded at both ends. Specifically, the manufacturing process involves: (1) welding one end of a length of titanium tubing having an outside diameter of 0.8 mm and a wall thickness of 0.05 mm; (2) inserting I-125 resin balls or an I-125 silver rod into the tube; and (3) welding the second open end. The resulting Seed length is about 4.5 mm. Weld thickness averages about 0.5 mm (approximately ten times the Seed wall thickness).

RATIONALE:

I-125 Seed have been welded using custom-built tungsten inert gas (TIG) welders since 3M's acquisition of this product line in 1978. Recently, a change to a plasma arc welding technique has been evaluated as an alternative to the TIG process, for the following reasons:

1. Both tungsten inert gas and plasma arc welders melt the tip of a titanium tube with an electrical current in an inert gas atmosphere. When the current ceases, the melt solidifies, producing a roughly spherical weld. Plasma arc welding produces a hotter melt temperature (50,000 degrees F. as opposed to 20,000 degrees F. for TIG) and is a more controlled process.

2. Plasma arc welding results in a more uniform weld thickness at both ends of the Seeds.

3. The custom TIG welders were requiring increased down-time for maintenance and repair. Purchase of replacement custom units was determined not to be a viable option because of obsolete welder design. Plasma arc welding allows us to establish a commercial supplier for state-of-the-art welding equipment.

4. Plasma arc welding provides an opportunity for semi-automation of the I-125 Seed welding processes, which is not possible with the TIG welders currently used.

Supporting documentation for this rationale presented below indicates that the plasma arc technique produces I-125 Seeds which are equivalent to TIG-welded Seeds in most respects and superior in terms of weld shape and uniformity of weld thickness.

COMPARATIVE EVALUATION OF I-125 SEEDS WITH TIG AND PLASMA ARC WELDING:

I-125 Seeds have been subjected to several tests to demonstrate that the plasma arc weld is an appropriate alternative to the tungsten-inert gas weld method. These procedures include: (1) visual inspection of weld thickness; (2) microvideography of welding process; (3) metallurgical analysis of welds; and (4) compressive sheer testing of welds. Detailed descriptions of these test procedures and resulting data/observations are presented below.

1. Visual Inspection of Weld Thickness

I-125 Seeds manufactured using either the TIG weld or plasma arc methods were evaluated visually for weld thickness. To estimate Seed weld thickness, a Polaroid X-ray of a group of Seeds was placed beneath a microscope having a 2.5 power objective lens with a 10 power Zeiss KPL-W-10X eye lens having a 100-division calibrated scale. Using dim external light, the photo was manipulated while looking through the eye-piece until the desired Seed weld was beneath the 100-division scale. An estimate was made (to the nearest 5 divisions or 75 μm) of the thickness of the Seed weld. Multiplying the number of divisions by a constant resulted in Seed thickness in microns. More recently, we have used a micrometer eye-piece which moves a hairline across the weld. Micrometer divisions moved, multiplied by a constant, relate to weld thickness in microns.

Results of these measurements are tabulated below for Seeds manufactured with either welding technique. Data are presented which summarize measurements for the thickness of the first weld of each capsule, the second weld, and the cumulative of the measurements. These data allow for comparison of thickness, resulting from the two welding techniques.

TABLE 1.

TYPICAL THICKNESS OF I-125 SEED WELDS IN MICRONS (μm)

	METHOD		
	Tungsten Inert Gas		
	1979	1988	Plasma Arc
1st and 2nd Weld			
N	100 welds	224 welds	120 welds
Mean (± 1 sd)	593 μm (116 μm)	616 μm (164μm)	513 μm (56 μm)
CV=SD/Mean x 100	19.6%	26.6%	10.9%
Range	250-850 μm	310-930 μm	368-624 μm
Range Spread	600 μm	620 μm	256 μm
1st Weld			
N	50 welds	112 welds	60 welds
Mean(± 1 SD)	672 μm (81 μm)	763 μm (77 μm)	555 μm (32 μm)
CV=SD/Mean x 100	12.1%	10.1%	5.8%
Range	450-850 μm	543-930 μm	548-624 μm
Range Spread	400 μm	387 μm	76 μm
2nd Weld			
N	50 welds	112	60 welds
Mean (± 1 SD)	517 μm (93 μm)	467 μm (72 μm)	470 μm (39 μm)
CV=SD/Mean x 100	18.0%	15.4%	8.2%
Range	250-750 μm	310-775 μm	368-536 μm
Range Spread	500 μm	465 μm	168 μm

These data indicate that, whether TIG or plasma arc welding is used, the resulting second weld is thinner than the first. The first weld tends to be convex on its outer and inner surface; the second weld will be convex on its outer surface but concave to flat on its inner surface. We hypothesize that this is due to a build-up in air pressure within the capsule.

When the average thicknesses of first and second TIG welds were compared for years 1979 and 1986, no statistical difference was found at the 0.01 level of significance. However, when the average thickness of first and second plasma arc welds were compared with either of the averages for TIG welds, a statistical difference was found at the 0.01 level of significance. The plasma arc welds were, on the average, thinner (by 45-111 μm) than the 1979 TIG welds and thinner (by 74 -136 μm) than the 1986 TIG welds at the 99% confidence level.

The statistically thinner average plasma arc weld results from a narrowing of the range of weld thicknesses, evidenced by comparing the "range" and "range spread" for the 1979 and 1986 TIG and plasma arc-welded Seeds. There are fewer thick welds in the latter Seeds, which reduces the average thickness.

The thinner average plasma arc-welded Seeds are suitable for clinical use, since weld thicknesses of about 500 um with NO variability are the desirable goal. The fact that plasma arc-welded thicknesses have less variability than TIG welds translates to an improved I-125 Seed with no net change to the Seed's performance in the hospital environment.

2. Microvideography of Welding Process

A high speed video camera was used to make a microvideography tape showing the magnified TIG and plasma arc welding processes in a total of 10 Seeds. Both first and second weld formations were taped. During normal playback, the welding process was observed in slow motion.

The TIG welding process was sporadic in the sense that an electrical discharge from a tungsten electrode struck a high point on the end of the titanium tube and sequentially worked its was across the lower portions of the top of the tube and down a portion of the tube wall. This resulted in a nonuniform weld puddle, which tended to produce tilted, bulbous (extend beyond the outer diameter of the titanium can) welds upon Seed cooling. Finished specs of I-125 Seeds accommodate the bulbous welds.

Microvideography also showed that TIG welding had a propensity to produce unfinished welds, resulting in Seed welds with holes and burrs. These Seeds are identified as rejects and culled during the quality control portion of the Seed manufacturing cycle.

Studies showed that, within certain limits, thickness of the weld was controlled by the length of titanium tubing exposed to the current. Welds thinner than about 0.25 mm could not be produced reliably.

In the plasma arc technique, by contrast, the current which flowed through the column of ionized argon gas surrounding the titanium tube end and length resulted in a uniform and controlled weld puddle. The puddle cooled to form a uniform and nearly non-bulbous weld. An even more uniform weld could be produced by pulsing the current at various pre-determined frequencies. Additional studies showed that weld thickness was controlled not only by the length of titanium tubing exposed to the current flowing through the ionized argon but also by the rate of gas flow and magnitude of the current. This greater flexibility allows thinner welds (to 0.1 mm) to be produced using the plasma arc technique, if such a product change is desired in the future.

3. **Metallurgical Analysis of Welds:**

Twenty-five (25) non-radioactive Seeds were made with one end welded by TIG and the other welded by plasma arc. From these, four Seeds were randomly selected to be mounted, cross-sectioned, polished, photographed, and evaluated.

Welds from both TIG and plasma arc processes were described by the 3M metallurgist conducting the study as having "full penetration" with no porosity or other flaws. The strength levels of both types of welds were predicted to be similar.

Crystal structure for TIG and plasma arc welds were described as typical of cast titanium. The TIG welds had a smaller grain size, thought to be caused by more rapid quenching of the molten metal due to a lower heat input.

4. **Compressive Shear Testing of Welds:**

Twenty (20) titanium tubes were welded ten each using TIG and plasma arc processes. Each respective Seed was held horizontally in a special jig so that an 0.8 mm length of Seed protruded; this amounted to all of the Seed weld and a short length of adjacent tubing. Using an Instron® apparatus to measure applied force, a metal bar was pushed down on the Seed, creating a scissors action which sheared the weld from the titanium tube. The resulting force, compressive shear, was measured in kg. Two samples of titanium tubing, not welded, were similarly tested.

Results of these measurements are tabulated below:

TABLE 2.

COMPRESSIVE SHEAR FORCES
I-125 SEED WELDS

Weld Type	Compressive Shear (kg) $\pm$ 1 SD
TIG	11.4 $\pm$ 0.8
Plasma Arc	12.0 $\pm$ 0.8
No weld, tubing only	6.5 $\pm$ 0.4

There was no statistical difference found in compressive shear for titanium tubes welded by TIG or plasma arc processes at the 0.01 level of significance. Tubing which has not been welded exhibits about half the compressive shear.

CONCLUSION:

Merrick Plasma Arc Welders have replaced Tungsten Inert Gas welders in the I-125 Seed production facility in New Brighton, MN. Comparative microvideography, weld thickness measurements, metallurgical weld analysis, and compressive shear tests have shown that plasma arc-welded Seeds are equivalent to TIG-welded Seeds in most aspects and are superior in terms of weld shape and uniformity of weld thickness.

(RESERVED)

Medical Product[illegible]sion/3M

3M Center
St. Paul, Minnesota 55144
612/733 1110

January 17, 1985

U.S. Nuclear Regulatory Commission
Region III
799 Roosevelt Road
Glen Ellyn, Illinois 60137
Attn: George M. McCann

Re: Materials License No. 22-00057-59MD
3M renewal application May 1, 1980

Dear Mr. McCann:

This letter is to provide revisions in the information originally submitted on May 1, 1980, as part of 3M renewal application for the license cited above. This includes a listing of page numbers affected and one set replacement pages incorporating the revisions.

If you have any questions regarding this submission, please feel free to contace me (612/733-6421).

Sincerely yours,

Jacquelyn A. Bush

Jacquelyn D. Bush
Manager, Regulatory Affairs
Medical Products Division/3M
3M Center, Bldg. 270-4A-05
St. Paul, MN 55144

JDB:kjh

Attachment

Jacquelyn D. Bush
Regulatory Affairs Manager

3M

Medical Products Division/3M

270-4A-05 3M Center
St. Paul, Minnesota 55144
612/733 6421

From the desk of

Jacquelyn D. Bush

1/18

Mike –

Here is the info about adding
ductilex, the new LTC
cancer, CLP and HER drugs.
All these drugs are associated
with the licinic renewal deal,
I've added them all together
for your convenience.

Looking forward to
hearing from you regarding
Vitas anticipation of
this change.

3M

(2) THE APPLICANT SUBMITS SUFFICIENT INFORMATION REGARDING EACH TYPE OF SOURCE OF DEVICE PERTINENT TO AN EVALUATION OF ITS RADIATION SAFETY, INCLUDING:

(i) The byproduct material contained, its chemical and physical form and amount.

Byproduct material: Iodine-125

Chemical form:

*Models 6701, 6702 - Iodide, as a part of a quaternary ammonium compound, namely Dowex^{R}21K (AG 21K) anion exchange resin.

Radioactive iodine-125 is affixed to the resin by simple ion exchange in an aqueous solution of pH>10

$$(\phi\text{-}CH_2N^+(CH_3)_3Cl^- + {}^{125}I^- \longrightarrow \phi\text{-}CH_2N^+(CH_3)_3{}^{125}I^- + Cl^-.)$$

Model 6711 - Silver iodide on a silver rod.

Radioactive iodine-125 is affixed to the silver rod coated with silver chloride by simple ion exchange in aqueous solution of pH $\geq$ 10, according to the reaction,

$$\text{silver rod/AgCl} + Na^{125}I \longrightarrow \text{silver rod/Ag}^{125}I + NaCl$$

Physical form:

Models 6701, 6702 - Solid spheres of $\phi\text{-}CH_2N^+(CH_3)_3{}^{125}I^-$ hermetically sealed within a titanium can.

*NOTE: Model 6701 I-125 Seeds have been deleted from the product line as of September 1, 1983, and have been replaced by Model 6711 Seeds. Since prototype tests were conducted on the Model 6701 Seed and not on the similar and still marketed 6702 Seed, however, descriptions of the Model 6701 Seed are retained in this license renewal application.

* 1-17 SE letter from S. Seal & Sh.

Model 6711 - Solid silver rod with adsorbed I-125 and hermetically sealed within a titanium can.

Amount:

Model 6702 contains a maximum of 50 mCi iodine-125 per source. Allowing for attenuation by the titanium capsule of 16%, the maximum effective output is 42 millicuries* of iodine-125.

Model 6711 contains a maximum of 100 mCi iodine-125 per source. Allowing for attenuation by the silver rod and titanium capsule of 35%, the maximum effective output of the model 6711 is 65 millicuries of iodine-125.

*NOTE: By "millicuries", we mean "apparent activity in millicuries". This is descriptive of output activity only and not the total quantity of I-125 contained within the titanium capsule of the Seed. Seeds are calibrated using I-125 Seed standards provided by the National Bureau of Standards (detailed discussion presented on page 149).

(iii) Procedures for, and results of, prototype tests to demonstrate that the source or device will maintain its integrity under stresses likely to be encountered in normal use and accidents.

I-125 Seeds have been subjected to four prototype tests to demonstrate that the sources maintain their integrity under stresses of use and accidents. These procedures are provided for source evaluation under the following stress conditions, along the lines of those suggested in NBS Handbook 126, ANSI N542-1977, Appendix C, and ANSI N44.1-1973: 1) autoclave, 2) impact, 3) percussion, and 4) bend.

Following each prototype test procedure, I-125 Seeds were subjected to a soak test, according to the following procedure. Each seed was placed into a 1 (one) dram vial (3.7 ml) containing 3.0 ml of a wash solution (0.01M NaI, 0.01M NaOH, and liquid detergent, preparation of which is described on page 136 of this submission.

The vial was closed using a screw cap and allowed to stand at ambient temperature for 12 to 20 hours. At this time, the vial supernatant was withdrawn from the seed and assayed for radioactivity using a Searle model 1195 automatic gamma counter with a sodium iodide well crystal. Each I-125 Seed was considered to have passed the prototype test described if removable activity was less than 0.005μCi.

The four prototype tests and resulting experimental data are described below. Seeds evaluated were of the models 6701 and 6711 configuration, with separate seeds evaluated in each test procedure.

Prototype Seeds were calibrated in terms of "mCi comp.", a measure of Seed output, using 3M-generated I-125 Seed standards. After September 1, 1983, I-125 Seeds are calibrated in terms of "apparent activity in mCi", using I-125 Seed standards provided by the National Bureau of Standards. This value also describes Seed output. The difference between "mCi comp." and "apparent activity in mCi" is 5%.

PREPARATION OF "SOAK TEST" SOLUTION FOR PROTOTYPE TESTS

This wash solution is approximately 0.01M NaI, 0.01 M NaOH, and has a detergent to solution ratio of 1:200. To prepare 20 liters, follow the procedures below. In addition, follow all normal chemical laboratory safety procedures. Be sure to wear a lab coat, latex gloves, and safety glasses, and do all work in a well-ventilated area.

a) Weigh out 30.0 ± .0 grams of sodium iodide (NaI). Transfer the NaI to a 20-liter container.

b) Weigh out 8.0 ± .3 grams of sodium hydroxide (NaOH). Transfer the NaOH to a graduated cylinder.

c) To the NaOH in the graduated cylinder, add 100 ± 5 ml of "Mr. Clean" liquid detergent.

d) Transfer the NaOH/"Mr. Clean" solution to the 20-liter container.

e) Dilute the mixture in the 20-liter container with distilled or de-ionized water to a total volume of 20 liters.

f) Mix the contents of the container.

Formula:		
	0.01M NaI	= 1.5 g/liter
	0.01M NaOH	= 0.4 g/liter
	0.5% detergent	= 5 ml/liter

(iv) For devices containing byproduct material, the radiation profile of the prototype device.

Dose rates for I-125 Seeds, models 6701, 6702 and 6711, have been determined on the basis of data gathered for the models 6701 and 6702 seeds, inasmuch as the output activities for all models are measured in "mCi comp.". Specifically, maximum radiation levels were measured at 5 and 30 cm from the external surface of the source, as described below.

Films (Kodak Type II) were contained within plastic holders (2-1/4 by 3/4") during exposure. Background radiation was maintained at <1% of the film exposure with appropriate radiation shielding. Two films were added as a control to measure background radiation levels and to check the manufacturer's film developing process.

Six (6) I-125 Seeds, ranging in activity from 0.30 mCi comp.* to 19.25 mCi comp., were used to ascertain exposure at 5 cm. Four (4) seeds (3.29 to 19.25 mCi comp.) were used to measure exposure at 30 cm. Exposure times ranged from 0.4 to 43 hours. Exposed films were developed and read by R. S. Landauer, Jr. & Company (Glenwood Science Park, Glenwood, Illinois). Results of these measurements, tabulated below, were corrected to Average Dose Rate (in mr/hr·mCi) and averaged. An accuracy of ± 15% was assured by the testing laboratory.

Distance from source	Average dose rate
5 cm	25 mr/hr·mCi
30 cm	0.53 mr/hr·mCi

On the basis of these data, the following dose rates can be expected for I-125 Seeds of minimum (0.1 mCi comp.) and maximum (40 mCi comp.) activity.

I-125 Seed activity	Average dose rates (mr/hr) at 5 cm	at 30 cm
0.1 mCi comp.	2.5	0.053
40 mCi comp.	1000	21.2

*See discussion of "mCi comp." on page 129.

(v) Details of quality control procedures to assure that production sources and devices meet the standards of the design and prototype tests.

All model 6702 and 6711 I-125 Seeds are subjected to quality control tests prior to their transfer to a licensed recipient. In-process tests include the following procedures, which are described in detail on the following pages.

Procedure name	Sample size	Specification
Visual inspection	100%	Uniform welds, no holes. Seed length 4.20-4.90 mm. Seed diameter 0.77-0.96 mm.
Initial leak test	100%	<0.005 μCi removable radioactivity.
Second leak test and autoclave	100%	<0.005 μCi removable radioactivity
Assay for radioactivity	100%	≥0.10 mCi comp. I-125 activity

Any I-125 Seeds not meeting the specifications described above are rejected.

Control tests, in addition to those listed above, are performed as a final quality control check. These tests include the following procedures.

Procedure name	Sample size	Specification
Final leak test	100%	<0.005 μCi removable radioactivity.
Visual inspection	According to Mil. Std. 105*, Level II, AQL 0.15	Length and width as specified above.
	According to Mil. Std. 105, Level II, AQL 1.0	Uniform welds, no holes

*A copy of Mil. Std. 105 is presented as Appendix A to this submission.

IN-PROCESS I-125 SEED INSPECTION PROCEDURE

MATERIALS/EQUIPMENT

Welded I-125 Seeds	In-Process Labels
Forceps	Shell Labels
Diameter Gauge	Lead Pigs
Length Gauges	Funnels
Glass vials	Glove Box

CAUTION: I-125 Seeds and vials of seeds must be handled with forceps.

I-125 SEED INSPECTION

1. Before starting inspection, check glove box to assure that there are no seeds from previous lot. Attach in-process label to outside surface of glove box, indicating date, status, and lot number of seeds to be inspected.

2. Check I-125 seeds in length gauges; place short seeds into a reject container and place long seeds into a reweld container.

3. Check I-125 seeds in diameter gauge and place diameter rejects into a diameter reject container.

4. Visually examine accepted seeds for quality of welds. Place visual rejects into a visual reject container.

5. Place accepted seeds into clean glass vials inside lead pigs and cover.

6. Discard rejected seeds in an appropriate container.

7. Transfer accepted seeds to "clean and leak test" box.

8. Record quantity of seeds rejected and accepted.

I-125 SEED CLEANING AND INITIAL LEAK TEST PROCEDURE

MATERIALS/EQUIPMENT

Welded Seeds	Pipet & Pipet Tips
Ultrasonic Bath	Liquid Waste Container ($CaSO_4$)
Vial Holding Racks	Solid Waste Container
Lead Pigs	Forceps- Vials
GM Probe/Meter	Clean Vials
Liquid Waste/Vacuum System	Cleaning Solution (page 141A)
Erlenmeyer Flask	Oxford Dispenser
Glove Box	Funnels

CAUTION: I-125 Seeds and vials of seeds must be handled with forceps.

NOTE: 1) Before starting cleaning and leak testing, check glove box to make sure there are no seeds from previous lot. Also, attach in-process label to glove box indicating date, status, lot number of seeds.
2) Using an I-125 standard solution, check efficiency of GM probe.

I-125 SEED CLEANING

1. Add cleaning solution to each vial of seeds (up to 50 seeds per vial).
2. Place vials of seeds in ultrasonic bath for minimum of 15 minutes.
3. Remove vials of seeds from ultrasonic bath and draw off cleaning solution into hot waste flask.

I-125 SEED LEAK TEST #1

1. Add cleaning solution to each vial of seeds.
2. Place vials in ultrasonic bath for 15-30 minutes.
3. Remove one vial at a time from bath and transfer solution in vial to clean vial using pipet.
4. Assay solution in vial to determine if vial contains >0.005μCi I-125 activity (which indicates a leaker).
5. Draw off solution into hot waste flask and place assay vial into solid waste container.

PREPARATION OF SOLUTION FOR I-125 SEED CLEANING & LEAK TESTING

This solution consists of 0.01M sodium hydroxide, 0.1M sodium thiosulfate, and 0.1% by weight of Pluronic F-68 detergent. To prepare 20 liters, follow the procedures below. In addition, follow all normal chemical laboratory safety procedures; Wear a lab coat, latext gloves, and safety glasses, and perform all work in a well-ventilated area.

a) Add deionized water to a 20 liter plastic container until it is half full.

b) Weigh 8.0 grams (± 0.3 grams) of sodium hydroxide on a balance and transfer to the container.

c) Weigh 316 grams (± 4 grams) of anhydrous sodium thiosulfate on a balance and transfer to the container.

d) Weigh 20 grams (± 0.5 grams) of Pluronic F-68 detergent powder on a balance and transfer to the container.

e) Swirl the solution in the container to mix ingredients.

f) Fill the container with deionized water to the 20 liter mark and mix by swirling the solution.

g) Observe the clarity and color of the solution. It should be transparent and colorless.

h) Label the container with the Lot Number and manufacturing date of the solution. The solution has an expiration date of three (3) months from time of manufacturing.

IN-PROCESS I-125 SEED LEAK TEST #2 AND AUTOCLAVE PROCEDURE

MATERIALS/EQUIPMENT

Ultrasonic Bath(2)	Liquid Waste Container ($CaSO_4$)
Autoclave	Solid Waste Container
Vial Holding Racks	Forceps - Vials
Leak Pigs	Clean Vials
Low Energy Gamma (LEG) Probe(2)	Cleaning Solution (page 141A)
Mini-scaler (2)	Oxford Dispenser
Liquid Waste/Vacuum System	Funnels
Erlenmeyer Flask	Pipet & Pipet Tips
Glove Box	Poly Bottle
Welded Seeds	D.I. Water

CAUTION: 1) I-125 Seeds and vials of seeds must be handled with forceps.
2) Surface of autoclave in thermally hot when operating. Do not touch.

NOTE: 1) Before starting leak testing and autoclaving procedure, check glove box to make sure there are no seeds from previous lot. Also, attach in-process label to glove box indicating date, status, lot number of seeds.
2) Using an I-125 standard solution, check efficiency of LEG probe weekly and record results in log book.

I-125 SEED LEAK TEST #2

1. Place up to 50 seeds into a vial and add cleaning solution.
2. Place vials in ultrasonic bath for 15-30 minutes.
3. Remove one vial at a time from bath and transfer solution in vial to a clean vial, using a pipet.
4. Assay solution in vial to determine if vial contains >0.005 μCi I-125 activity (which indicates a leaker).
5. Draw off solution into hot waste flask and place assay vial into solid waste container.
6. Place vials containing non-leaking seeds into OK rack and vials containing leaking seeds into a leaker rack.

(RESERVED)

I-125 SEED ASSAY-CALIBRATION PROCEDURE

MATERIALS/EQUIPMENT

Cabintec CRC-7R Radioisotope Calibrator	NBS I-125 Seed Standards
Seed holding "wand"	I-125 Seeds For Assay
Storage Cabinet	Am-241 Check Source
Forceps	Lead Pigs
Lead Filled Gloves	Safety Gloves
Labels	

CAUTION: 1) Handle I-125 Seeds and vials of Seeds with forceps.

2) Wear Lead filled gloves and safety glasses.

3) Perform all assay work behind L-Block.

ASSAY PROCEDURE

1. Switch Capintec "on" 24 hours prior to initial assay session and allow unit to remain on continuously.

2. Set "zero" and "background" reading to 00.00 on the digital display.

3. Insert Am-241 check source into the Capintec ionization well and record digital reading. Ensure that the reading falls within +/- 1% of the designated value. Remove check source.

4. Insert the correct I-125 Seed Standard* into the "wand". Insert the wand into the Capintec ionization well, and record the digital "mCi" reading. Ensure that the reading falls within +/- 2% of the Seed's current value obtained from a decay table. Remove Standard Seed.

5. Place a Seed to be assayed into the wand. Insert the wand into the Capintec ionization well. Observe the digital "mCi" reading.

6. Dump the assayed Seed from the wand into one of several lead pigs identified with different millicurie activity ranges.

7. Repeat Steps 5 & 6 until all Seeds have been assayed.

8. Count Seeds in each of the activity ranges and record this information on labels affixed to the lead pigs.

9. Place lead pigs into the inventory cabinet.

*NBS Standards exist for Model 6702 and 6711 I-125 Seeds. Standards and Seeds to be assayed must be of the same Model.

Q.C. I-125 SEED FINAL LEAK TEST PROCEDURE

MATERIALS/EQUIPMENT

- L-Block
- Forceps
- Clean Vials
- Ultrasonic Bath
- Mini-Scaler
- Low Energy Gamma (LEG) Probe
- I-125 Seeds
- Cleaning Solution (page 141A)
- Distilled Water
- Lead Pigs
- Vial Holder
- Leak Hand Gloves
- Safety Glasses

CAUTION: 1) I-125 Seeds and vials of seeds must be handled with forceps.
2) Lead hand gloves and safety glasses must be worn when working at this station.
3) All work is performed behind L-Block in fume hood.

NOTE: Using an I-125 standard, check efficiency of counting system prior to each leak test and record results in log book.

FINAL LEAK TEST PROCEDURE

1. Place seeds (not more than 500) into glass vial and immerse with cleaning solution and allow to soak overnight.
2. Place vial of seeds into ultrasonic bath for not more than 10 minutes.
3. Remove vial of seeds from bath and transfer solution in vial to clean vials.
4. Assay solution in vials to determine if vial contains >0.005 µCi I-125 activity (which indicates a leaker). If a leaker is detected, that vial is quarantined until it is sorted and defective seed(s) are removed. The balance of the seeds are again subjected to the leak test.
5. Record assay results.
6. Rinse I-125 Seeds in vials with distilled water and acetone and then dry.
7. Place dry seeds in a vial in lead container and label with in-process label.

Q.C. I-125 SEED INSPECTION PROCEDURE

MATERIALS/EQUIPMENT

- Welded I-125 Seeds
- Forceps
- Diameter Gauge
- Length Gauge - Go/NoGo
- Magnifying Lens
- Lead Gloves
- In-Process labels
- Clean Vials
- L-Block
- Lead Pigs
- Funnels

CAUTION: I-125 Seeds and vials of seeds must be handled with forceps.

I-125 SEED MAJOR DEFECT INSPECTION (Mil. Std. 105, Level II, AQL 0.15)

1. Check I-125 Seeds in length gauge; place defective seeds into a reject container.
2. Check I-125 Seeds in diameter gauge and place defective seeds into the same reject container.
3. Count the total number of defective seeds. If this number is greater than allowed by the sampling plan, reject the lot of seeds to production for corrective action.

I-125 SEED MINOR DEFECT INSPECTION (Mil. Std. 105, Level II, AQL 1.0)

1. Visually examine seeds using magnifying lens for quality of welds.
2. Place visual defects into a reject container. Count the total number of defective seeds. If this number is greater than allowed by the sampling plan, reject the lot of seeds to production for corrective action.
3. Place accepted seeds into vial and return to production for assay.
4. Record quantity of seeds acceptable and defective.

(vi) Procedures and Standards for calibrating sources and devices.

I-125 SEED STANDARDS

Model 6702 and 6711 Seed Standards are obtained from the National Bureau of Standards (NBS) at approximately six (6) month intervals. Calibration is stated in terms of exposure rate at one meter transverse to the axis of the Seed corrected for attenuation in air.

We convert exposure rate values to "apparent activity in millicurie" values using an exposure rate constant for I-125 of 1.45 r cm/h mCi as found in C.A. Sondhaus, in MODERN INTERSTITIAL AND INTRACAVITARY AND RADIATION CANCER MANAGEMENT, edited by Frederick W. George III, (Masson Publishing USA, Inc., New York, 1982), Chapter 9, p. 89. The mCi values represent "output" activity only and do not reflect I-125 contained within the Seeds. At present, source output is the relevant quantity used in dosimetry calculations for I-125 Seed implants*.

For each Standard, a decay Table is generated by computer. The Tables are posted near the Capintec CRC-7R assay instrument.

The Standards are stored in labeled lead pigs during their useful lives.

CALIBRATION INSTRUMENT/ASSAY METHOD

Production Model 6702 and 6711 I-125 Seeds are assayed in fixed geometry using a Capintec CRC-7R Radioisotope Calibrator which has been adjusted to conform to the mCi values of the NBS Seed Standards (see p. 145 for the detailed assay procedure). The Calibrator uses a deep well ionization chamber having inside dimensions of 26cm high by 7cm in diameter.

We studied the well to determine the geometrically insensitive location for an I-125 Seed aligned vertically with the axis of the well. This was done by glueing a strand of thread to one end of a Seed and by raising the Seed at one (1) cm increments from the bottom of the well, noting the digital output readings on the instrument. By utilizing a plastic straw and circular cardboard cutouts, a four (4) cm distance along the axis which produced a constant reading. We chose the center of this plateau (about 9 cm from the well bottom) to position Production Seeds for assay. This study was repeated several times with similar results. An aluminum "wand" was fabricated to position Production Seeds at this insensitive location within the well.

The linearity of the instrument was ascertained by following the decay of Tc-99m and by comparing the observable decay with the calculated decay using a 6.02 hour half-life for the nuclide. Instrument linearity is checked at least once yearly.

We routinely use an Am-241 "constancy" check source in the ionization well to insure that the instrument's output reading is constant from day to day. This is a 14 mCi "window" source sealed in a welded stainless steel capsule, 10 mm long by 3 mm in diameter from Amersham, Code AMC.24. We determined the geometrically insensitive location for it along the axis of the well and fabricated a "wand" to hold it in fixed position.

I-125 SEED CLASSIFICATION

Model 6711 I-125 Seeds are assayed and then classified into logarithmically-arranged groups to allow for uniform decay accounting methods based on seven-day time increments. The activity ranges specified below are an example of typical ranges calculated in this manner.

Activity Range (mCi)
1.05+ -
.97 - 1.04
.89 - .96
.82 - .88
.76 - .81
.70 - .75
.65 - .69
.60 - .64
.55 - .59
.51 - .54
.47 - .50
.43 - .46
.40 - .42
.37 - .39
.34 - .36
.31 - .33

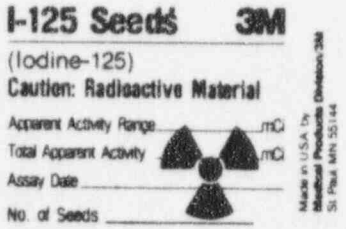
Model 6702 I-125 Seeds are assayed as described, and grouped into activity ranges specified by the user.

*It is recognized that "apparent activity" and the exposure rate constant are dummy variables which are eventually factored out in absorbed dose calculations. It is also realized that there is a trend toward source strength specification in terms of exposure rate or absorbed dose rate at a certain distance from the source. Nevertheless, to permit continued use of existing dosimetry protocols, we decided to adopt the convention "apparent millicurie", at least for the present. Modification of this description of Seed strength will be considered as warranted by future development in various aspects of medical physics relative to brachytherapy dosimetry.

(RESERVED)

(vii) Legend and methods for labeling sources and devices as to their radioactive content.

Because of the small size of I-125 Seeds, it is not possible to label each source as to its radioactive content. I-125 Seeds supplied as a group of seeds with an assay within a stated range on the assay date, are packaged in a 1 dram, screw cap glass vial, onto which is affixed a label stating radioactive content, a sample of which is attached below. This label displays the caution symbol and is printed in colors to comply with the provisions of 10 CFR 32.72 and 10 CFR 20.203.



(viii) Instructions for handling and storing the source or device from the radiation safety standpoint; these instructions are to be included on a durable label attached to the source or device or attached to a permanent storage container for the source or device; provided, that instructions which are too lengthy for such label may be summarized on the label and printed in detail on a brochure which is referenced on the label.

The labeled vial containing I-125 Seeds is placed in a lead storage/shipping container, a schematic diagram for which is presented on pages 155 as Figures 4-4. Instructions for handling and storing the I-125 Seeds are summarized on a label affixed to the lead containers, samples of which are presented below for the models 6702 and 6711. These labels display the caution symbol and are printed in colors to comply with the provisions of 10 CFR 32.72 and 10 CFR 20.203. Detailed instructions for handling and storing seeds are presented in the I-125 Seed package inserts which are referenced on the lead container label. One copy of the appropriate package insert is supplied for each vial of I-125 Seeds in a shipment. Copies of the three package inserts are presented on pages 165-174 of this submission.

I-125 Seeds

3M

Therapeutic For Interstitial Brachytherapy No. 6702

Made in U.S.A. by
Radiation Therapy Products
Medical Products Division/3M
St. Paul, MN 55144

DESCRIPTION: I-125 Seeds consist of a welded titanium capsule containing iodine-125 adsorbed on anion exchange resin spheres.

Apparent activity range _____ mCi

Total apparent activity this vial _____ mCi

Number of seeds _____ Assay Date _____

Lot No. _____

See package insert for instructions on handling and storage of I-125 Seeds.

Caution Radioactive Material

WARNING Licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to § 35.14 and § 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States.
CAUTION Federal law restricts this device to sale by or on the order of a physician. Maintain proper radiation safety precautions at all times.

11-82

Label for Lead Storage/Shipping Container - Model 6702

I-125 Seeds

3M

Therapeutic For Interstitial Brachytherapy No. 6711

Made in U.S.A. by
Radiation Therapy Products
Medical Products Division 3M
St. Paul, MN 55144

DESCRIPTION: I-125 Seeds consist of a welded titanium capsule containing iodine-125 adsorbed onto silver rod.

Apparent activity range _____ mCi

Total apparent activity this vial _____ mCi

Number of seeds _____ Assay Date _____

Lot no. _____

See package insert for instructions on handling and storage of I-125 Seeds.

Caution Radioactive Material

WARNING Licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to § 35.14 and § 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States.
CAUTION Federal law restricts this device to sale by or on the order of a physician. Maintain proper radiation safety precautions at all times. 11-82

Label for Lead Storage/Shipping Container - Model 6711

(RESERVED)

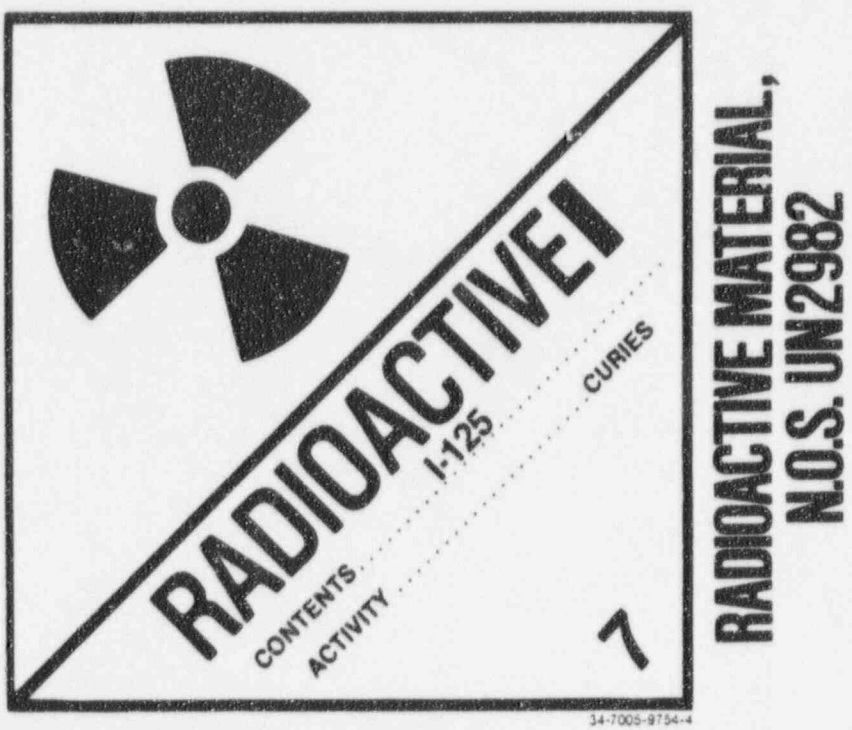
The labeled lead container is then placed in a U.S.A. DOT 7A, Type A cardboard shipping container, lined with styrofoam. One certification sheet (page 175), the appropriate number of package inserts, and a WARNING statement about Seed handling (presented below) are included with each shipment, and the box is sealed with suitable packaging tape.

Warning:

Do not force I-125 seeds into (or out of) any implant tube, needle, or cartridge. Doing so may damage the wall or end welds of the seed potentially causing release of I-125 into body fluids if the seed is implanted. If an I-125 seed has been visibly damaged in any way, discard it immediately to radioactive waste and check the area for contamination. Under no circumstances should a visibly damaged seed be implanted.

34-7015-0734-4

The sealed shipping carton, identified with the phrases "U.S.A. DOT 7A Type A" and "Radioactive Material N.O.S.", is then labeled with the label attached below.



34-7005-9754-4

I-125 Seeds are used for the interstitial treatment of cancers and, as such, are placed directly into the tumor to be irradiated. The placement of I-125 Seeds in tissue, which takes place in a surgery, is facilitated by the use of one of several commercially-available implant tools. These implanters are used solely for source placement and are not designed either to store or to hold I-125 Seeds, as is the case with conventional applicators and cesium-137 sources. Instructions for handling and storing the I-125 Seeds are presented in the package inserts for the product (pages 165-174).

(RESERVED)

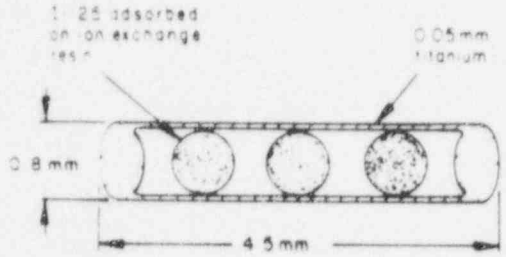
(RESERVED)

(RESERVED)

I-125 Seeds
No. 6702

Description

I-125 Seeds 6702 consist of a welded titanium capsule containing Iodine-125 adsorbed on anion exchange resin spheres.



Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic photons and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal photon emissions are 27.4 and 35.5 keV x-rays and a 35.5 keV gamma.

To correct for the physical decay of Iodine-125, the decay factors at selected days after the assay date are shown in the table below.

Decay Chart Iodine-125, Half Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
0	1.000	36	0.661
2	0.977	38	0.646
4	0.955	40	0.631
6	0.933	42	0.617
8	0.912	44	0.603
10	0.891	46	0.589
12	0.871	48	0.575
14	0.851	50	0.562
16	0.832	52	0.550
18	0.813	54	0.537
20	0.794	56	0.525
22	0.776	58	0.513
24	0.759	60	0.501
26	0.741	62	0.490
28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for Iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit 27.4 and 35.5 keV x-rays and a 35.5 keV gamma. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility and results in a total self-absorption of approximately 16%.

Indications

I-125 Seeds are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, and moderate radiosensitivity.

I-125 Seeds may be used for selected radiation applications as removable implants.

I-125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (eg, ulcerated) is not recommended with I-125 Seeds.

Warnings

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

Precautions

Preparation for Use/Sterilization

I-125 Seeds are radioactive and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel, consistent with published exposure limits.

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body and for handling, a ring badge will provide adequate detection.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121° C at 15 psi to 138° C at 35 psi. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138° C and 35 psi).

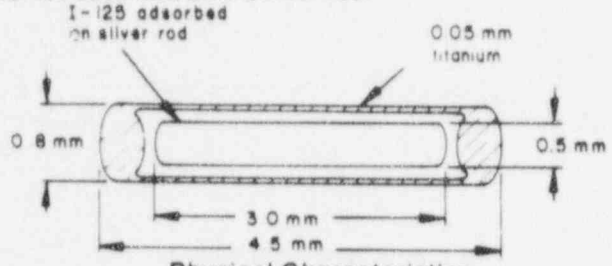
I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and teflon. I-125 Seeds may also be autoclaved in selected accessories to commercially-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun and nylon and teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion or inhalation of Iodine-125.

I-125 Seeds
No. 6711

Description

I-125 Seeds 6711 consist of a welded titanium capsule containing iodine-125 adsorbed onto a silver rod.



Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic x-rays and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal radiation emissions are x-rays of 27.4 keV and 35.5 keV.

To correct for the physical decay of Iodine-125, the decay factors at selected days after the assay date are shown in the table below.

Decay Chart Iodine-125, Half Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
0	1.000	36	0.661
2	0.977	38	0.646
4	0.955	40	0.631
6	0.933	42	0.617
8	0.912	44	0.603
10	0.891	46	0.589
12	0.871	48	0.575
14	0.851	50	0.562
16	0.832	52	0.550
18	0.813	54	0.537
20	0.794	56	0.525
22	0.776	58	0.513
24	0.759	60	0.501
26	0.741	62	0.490
28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit x-rays of 27.4 and 35.5 keV. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility, and together with the silver rod, results in a total self-absorption of approximately 35%.

Indications

I-125 Seeds with apparent activities from 0.1 to 1.0 mCi are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, slow growth rate, and low to moderate radiosensitivity. Seeds in this apparent activity range may be used to treat superficial, intraabdominal, and intrathoracic tumors. Tumors of the head, neck, lung, pancreas, and prostate (early stages) are commonly treated.

125 Seeds with total apparent activities greater than 1.0 mCi are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, and moderate radiosensitivity. These seeds may be used for selected radiation applications as removable implants.

I-125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (e.g. ulcerated) is not recommended with I-125 Seeds.[1]

Warnings

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

Precautions

Preparation for Use/Sterilization

I-125 Seeds are radioactive, and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel consistent with published exposure limits.[2]

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body and, for handling, a ring badge will provide adequate monitoring.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121° C at 15 psi to 138° C at 35 psi. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138° C and 35 psi).

I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and Teflon. I-125 Seeds may also be autoclaved in selected accessories to commerically-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun, and nylon and Teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures, or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container, and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion, or inhalation of iodine-125.

(RESERVED)

(RESERVED)

(RESERVED)

Medical Products Division/3M

3M Center
St. Paul, Minnesota 55144
612/733 1110

3M

January 11, 1983

U. S. Nuclear Regulatory Commission
License Management Branch
Division of Fuel Cycle and Material Safety
Washington, D. C. 20555

Attention: Joseph DelMedico

Re: Materials License No. 22-00057-59 MD

Dear Mr. DelMedico:

This letter is to advise you of changes that we plan to make in the quality control procedure for I-125 Seeds, 3M Models 6701, 6702, and 6711, listed on Materials License No. 22-00057-59 MD, amendment 04. These changes necessarily apply to model 6720, since it is a device incorporating model 6701 or 6711 I-125 Seeds. Specifically, these changes represent a revised procedure for calibrating I-125 Seeds, with a concommitant change in the nomenclature used to describe seed radioactivity.

The assay procedure described in previous license amendment applications consisted of using a Victoreen condensor-R-meter from which 3M primary I-125 Seeds standards were prepared for the routine calibration of production assay equipment. This procedure represented the state-of-the-art at that time, due to the unavailability of an appropriate I-125 Seed standard from the National Bureau of Standards (NBS).

The desirability of having an I-125 Seed standardized by the NBS and manageable nomenclature was apparent. To this end, we have been collaborating for the past three years with NBS in a standards development program. As a result, now available to us are appropriate NBS standards for our three I-125 Seeds sources.

These NBS-generated, standardized sources enable us to improve the calibration of assay equipment, thereby improving the assay of the products. An additional benefit is an improvement in the nomenclature used to describe the strength of the source. The term "millicuries/Compensated", currently used to describe seed output, will be replaced by a more descriptive and less confusing term, "apparent activity in millicuries." These revisions are described in detail in the following attachments to this letter,

which revise items 2(vi), 2(vii), and 2(viii), of the files dated July 26, 1979, July 29, 1980 and May 1, 1981 for I-125 Seeds 6701 and 6702, 6711, and 6720 respectively:

Attachment A - Procedures and Standards for Calibrating Sources and Devices, plus Appendix C.

Attachment B - Legend and Method for Labeling Sources and Devices.

Attachment C - Instructions for Handling and Storing the Source and Device.

These changes in the calibration procedure and nomenclature in no way alter the composition of the products, their radioactive strength (i.e. millicurie content), or recommended handling of these products. Indeed, they advance the state-of-the-art for health care professionals using I-125 Seeds, by providing them with a clearer representation of each source's radioactivity. We feel that the benefits afforded the user by these changes are significant and, as such, we would appreciate your expeditious review of this submission. Our plans are to implement these changes during the second quarter of 1983.

If you have any questions regarding the information presented herein, please feel free to contact me (612/733-6421).

Sincerely yours,

Jacquelyn D. Bush

Jacquelyn D. Bush
Supervisor, Regulatory Affairs
Medical Products Division/3M
3M Center, Bldg. 270-4A-05
St. Paul, Minnesota 55144

JDB/CWO/tmf

Attachments

Attachment A

(vi) Procedures and Standards for

Calibrating Sources and Devices

Revised 12/17/82

(vi) Procedures and Standards for calibrating sources and devices.

Each model No. 6701, 6702, and 6711 I-125 Seed is assayed using a meter equipped with either a sodium iodide (well) crystal or a plastic scintillation crystal or by using a standard isotope calibrator (such as marketed by Searle and RADX) having a well re-entrant ionization chamber. When using the well sodium iodide crystal or the well ionization chamber, the I-125 Seed is centrally positioned in a fixed geometry within the well. When using the plastic scintillation crystal, the Seed is positioned in a fixed geometry with its long axis parallel to the internal face of a slot machined within the plastic crystal.

These assay systems are calibrated using three (3) I-125 Seed standards which bracket the activity range of the I-125 Seeds being assayed. At least one of the seed standards is a 3M primary standard calibrated by the National Bureau of Standards (NBS). The others are 3M secondary standards prepared by us from the primary one. Preparation, maintenance and use of the I-125 Seed standards is described in Appendix C.

The I-125 Seeds are assayed and then classified into logarithmically-arranged groups to allow for uniform accounting methods based on seven-day time increments. The activity ranges specified below are an example of typical ranges calculated in this manner.

Apparent Activity Range in mCi

1.05+
.97 - 1.04
.89 - .96
.82 - .88
.76 - .81
.70 - .75
.65 - .69
.60 - .64
.55 - .59
.51 - .54
.47 - .50
.43 - .46
.40 - .42
.37 - .39
.34 - .36
.31 - .33

These ranges are based on the arithmetic mode selling range of 0.55 - 0.59 mCi. These activity ranges can be ordered to correspond to a different arithmetic mode as required by the customer. I-125 Seeds with activities greater than 1.05 mCi are similarily grouped into selected ranges.

The phrase "apparent activity in millicuries" is meant to convey source output rather than activity contained within the titanium capsule of the I-125 Seed. At present, source output is the relevant quantity used in dosimetry calculations for I-125 Seed implants.

Revised 12/17/82

Appendix C

Procedures and Standards for Calibrating I-125 Seeds

Revised 12/17/82

Preparation

Maintenance and Use of I-125 Seed Calibration

Sources

A. Primary I-125 Seed Standards

I-125 Seed standards are maintained for cross-calibration and assay of Production Seeds at the New Brighton manufacturing facility. A standard set consists of three (3) I-125 Seeds, selected in such a manner so as to represent normal activity ranges for Seeds being sold.

Two (2) I-125 Seeds (A and B) are submitted to the NBS for calibration every six months. At the time of this calibration, seed A occupies the highest activity position of the bracketed range. It is used as it decays, passing from position No. 1 through lower activity positions no. 2 and 3 until it decays below the bracketed range at the beginning of the fourth month. At this time NBS seed standard B assumes position no. 1, following the same decay route until it is replaced with another seed A on a new set of NBS standards at the beginning of the seventh month.

3M secondary I-125 Seed standards are prepared from the 3M primary NBS Seeds according to the procedure described below, to fill positions not occupied by the primary seeds. For example, when NBS standard A fills positions no. 1, secondary standards will fill positions no. 2 and no. 3. As standard A decays to position no. 2, secondary standard no. 3 will drop from the bracketed range and a new secondary standard is prepared to fill vacant position no. 1.

A computer-generated decay chart is prepared for each primary or secondary I-125 Seed standard to follow its decay through the three positions within the bracketed range.

B. Secondary I-125 Seed Standards

Secondary I-125 Seed standards are generated from the primary standard by comparing output values using one or more of three (3) different measurement systems:

1. A Victoreen condensor-R-meter (model 570-5) and a 0.25R ionization chamber (model 130) with the seeds maintained in a fixed geometry at the end of the ionization chamber. A constancy check of this measurement system is performed using a 14 mCi Am-241 "point" source from Amersham Corp. (3mm diameter by 10mm long with a 0.2 mm thick window).

2. A Searle Isotope Calibrator (model CRC-22NB) with a well re-entrant ionization chamber. A constancy check of this instrument is performed using a 3M Cs-137 medical source (20mm long by 3.1mm diameter and 14 mm active length) having an activity range from 1 to 10 mCi.

3. A Tracor Northern (TN 1705) pulse height analyzer (PHA) with a 3 inch diameter sodium iodide (well) detector. The constancy of this instrument is assessed using a 3 mCi AM-241 "point" source from Amersham Corp. (2mm diameter by 10 mm long with a .02mm thick window).

C. Specification of I-125 Seed Strength

I-125 Seed standards are calibrated by the NBS in a direction transverse to the axis of the seed and are typically specified in units of $nR \cdot m^2/s$ corrected for attenuation in air. To obtain seed strength in terms of apparent activity in mCi* we divide the specified output from the NBS Seed standards by the exposure rate constant for I-125 at one meter.**

---

* It is recognized that "apparent activity" and the exposure rate constant are dummy variables which are eventually factored out in absorbed dose calculations. It is also realized that there is a trend toward source strength specification in terms of exposure rate or absorbed dose rate at a certain distance from the source. Nevertheless, to permit continued use of existing dosimetry protocols, we decided to adopt the convention "apparent millicurie", at least for the present. Modification of this description of seed strength will be considered as warranted by future development in various aspects of medical physics relative to brachytherapy dosimetry.

** An exposure rate constant of 40.3 nR· m^2/s·mCi (1.45 R· cm^2/h·mCi) as found in C.A. Sondhaus, in Modern Interstitial and Intracavitary Radiation Cancer Management, edited by Frederick W. George III, (Masson Publishing USA, Inc., New York, 1981) Chap, 9, p. 89.

Attachment B

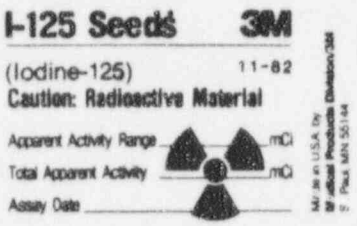
(vii) Legend and Methods for Labeling Sources and Devices

As To Their Radioactive Content

Revised 12/30/82

(vii) Legend and methods for labeling sources and devices as to their radioactive content.

Because of the small size of I-125 Seeds, it is not possible to label each source as to its radioactive content. I-125 Seeds supplied as a group of seeds with an assay within a stated range on the assay date, are packaged in a 1 dram, screw cap glass vial, onto which is affixed a label stating radioactive content, a sample of which is attached below. This label displays the caution symbol and is printed in colors to comply with the provisions of 10 CFR 32.72 and 10 CFR 20.203.



Attachment C

(viii) Instructions for Handling and Storing the Source or Device

Revised 12/30/82

(viii) Instructions for handling and storing the source or device from the radiation safety standpoint; these instructions are to be included on a durable label attached to the source of device or attached to a permanent storage container for the source or device; provided, that instructions which are too lengthy for such label may be summarized on the label and printed in detail on a brochure which is referenced on the label.

The labeled vial containing I-125 Seeds is placed in either one of two lead storage/shipping containers. Instructions for handling and storing the I-125 Seeds are summarized on a label affixed to the lead containers, samples of which are presented below. These labels display the caution symbol and are printed in colors to comply with the provisions of 10 CFR 32.72 and 10 CFR 20.203. Detailed instructions for handling and storing seeds are presented in the I-125 Seed package inserts, which are referenced on the lead container label. One copy of the package insert, presented on the following pages, is supplied for each vial of I-125 Seeds in a shipment.

I-125 Seeds **3M**

Therapeutic For Interstitial Brachytherapy No. 6701

Made in U.S.A. by
Radiation Therapy Products
Medical Products Division/3M
St. Paul, MN 55144

DESCRIPTION: I-125 Seeds consist of a welded titanium capsule containing one gold sphere and Iodine-125 adsorbed on two anion exchange resin spheres.

Apparent activity range: ___ _____ mCi

Total apparent activity this vial: _____ mCi

Number of seeds: _____ Assay Date: _____

Lot no. _____

See package insert for instructions on handling and storage of I-125 Seeds.

Caution Radioactive Material

WARNING Licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to § 35.14 and § 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States. **CAUTION** Federal law restricts this device to sale by or on the order of a physician. Maintain proper radiation safety precautions at all times.

11-82

Label for Lead Storage/Shipping Container - Model 6701

I-125 Seeds

3M

Therapeutic For Interstitial Brachytherapy No. 6702

Made in U.S.A. by
Radiation Therapy Products
Medical Products Division/3M
St. Paul, MN 55144

Caution
Radioactive
Material

DESCRIPTION: I-125 Seeds consist of a welded titanium capsule containing iodine-125 adsorbed on anion exchange resin spheres.

Apparent activity range _____ mCi

Total apparent activity this vial _____ mCi

Number of seeds _____ Assay Date _____

Lot no. _____

See package insert for instructions on handling and storage of I-125 Seeds.

WARNING Licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to § 35.14 and § 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States.
CAUTION Federal law restricts this device to sale by or on the order of a physician. Maintain proper radiation safety precautions at all times.

11-82

Label for Lead Storage/Shipping Container - Model 6702

I-125 Seeds

3M

Therapeutic For Interstitial Brachytherapy No. 6711

Made in U.S.A. by
Radiation Therapy Products
Medical Products Division/3M
St. Paul, MN 55144

Caution
Radioactive
Material

DESCRIPTION: I-125 Seeds consist of a welded titanium capsule containing iodine-125 adsorbed onto silver rod.

Apparent activity range _____ mCi

Total apparent activity this vial _____ mCi

Number of seeds _____ Assay Date _____

Lot no. _____

See package insert for instructions on handling and storage of I-125 Seeds.

WARNING Licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to § 35.14 and § 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States.
CAUTION Federal law restricts this device to sale by or on the order of a physician. Maintain proper radiation safety precautions at all times. 11-82

Label for Lead Storage/Shipping Container - Model 6711

Revised 12/17/92

I-125 Seeds®

3M

In Carrier Therapeutic For Interstitial Brachytherapy

No. 6720

Description: I-125 Seeds in Carrier consists of a group of I-125 Seeds housed at the fixed spacing indicated (center to center) within a braided absorbable carrier. The I-125 Seeds consist of a welded titanium capsule containing iodine-125 absorbed onto a silver rod. The carrier material is Ethicon no. 1 Vicryl® synthetic absorbable suture (Polyglactin 910).

Apparent activity range: _____ mCi

Total apparent activity _____ mCi

Number of seeds _____ Assay Date _____

Lot no. _____ Spacing _____

See package insert for instructions on handling and storage of I-125 Seeds in carrier.

Made in U.S.A. by
Radiation Therapy Products
Medical Products Division 3M
St. Paul, MN 55144

Caution
Radioactive
Material

WARNING Licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to § 35.14 and § 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States. **CAUTION** Federal law restricts this device to sale by or on the order of a physician. Maintain proper radiation safety precautions at all times. 11-82

S

Label for Lead Storage/Shipping Container - Model 6720

The labeled lead container is then placed in a U.S.A. DOT 7A, Type A cardboard shipping container, lined with styrofoam. One certification sheet (sample attached) and the appropriate number of package inserts are included with each shipment, and the box is sealed with suitable packaging tape.

Revised 12/17/82

PACKAGE INSERTS

FOR

I-125 Seeds^{R}

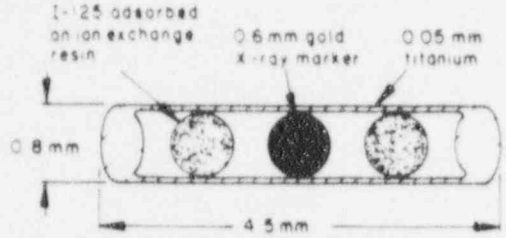
Models 6701, 6702, 6711 and 6720

Revised 12/17/82

I-125 Seeds
No. 6701

Description

I-125 Seeds 6701 consist of a welded titanium capsule containing Iodine-125 adsorbed on two anion exchange resin spheres. A spherical gold x-ray marker is included, which serves as a means of visualization on radiographs.



Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic photons and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal photon emissions are 27.4 and 35.5 keV x-rays and a 35.5 keV gamma.

To correct for the physical decay of Iodine-125, the decay factors at selected days after the assay date are shown in the table below.

Decay Chart Iodine-125, Half Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
0	1.000	36	0.661
2	0.977	38	0.646
4	0.955	40	0.631
6	0.933	42	0.617
8	0.912	44	0.603
10	0.891	46	0.589
12	0.871	48	0.575
14	0.851	50	0.562
16	0.832	52	0.550
18	0.813	54	0.537
20	0.794	56	0.525
22	0.776	58	0.513
24	0.759	60	0.501
26	0.741	62	0.490
28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for Iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit 27.4 and 35.5 keV x-rays and a 35.5 keV gamma. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility and results in a total self-absorption of approximately 16%.

Indications

I-125 Seeds are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, slow growth rate, and low to moderate radiosensitivity.

I-125 Seeds may be used to treat superficial, intraabdominal or intrathoracic tumors. Tumors of the head, neck, lung, pancreas, and prostate (early stages) are commonly treated.

I-125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (eg, ulcerated) is not recommended with I-125 Seeds.

Warnings

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

Precautions

Preparation for Use/Sterilization

I-125 Seeds are radioactive and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel, consistent with published exposure limits.

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body, and for handling, a ring badge will provide adequate detection.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121° C at 15 psi to 138° C at 35 psi. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138° C and 35 psi).

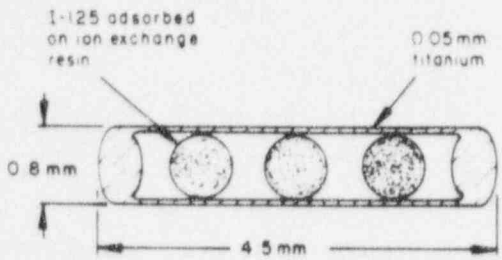
I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and teflon. I-125 Seeds may also be autoclaved in selected accessories to commerically-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun and nylon and teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Although I-125 Seeds have a high structural integrity, it is possible through rough handling, high temperatures or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion or inhalation of Iodine-125.

I-125 Seeds
No. 6702

Description

I-125 Seeds 6702 consist of a welded titanium capsule containing Iodine-125 adsorbed on anion exchange resin spheres.



Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic photons and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal photon emissions are 27.4 and 35.5 keV x-rays and a 35.5 keV gamma.

To correct for the physical decay of Iodine-125, the decay factors at selected days after the assay date are shown in the table below.

Decay Chart Iodine-125, Half Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
0	1.000	36	0.661
2	0.977	38	0.646
4	0.955	40	0.631
6	0.933	42	0.617
8	0.912	44	0.603
10	0.891	46	0.589
12	0.871	48	0.575
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26	0.741	62	0.490
28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for Iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit 27.4 and 35.5 keV x-rays and a 35.5 keV gamma. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility and results in a total self-absorption of approximately 16%.

Indications

I-125 Seeds are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, and moderate radiosensitivity.

I-125 Seeds may be used for selected radiation applications as removable implants.

125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (eg, ulcerated) is not recommended with I-125 Seeds.[1]

Warnings

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

Precautions

Preparation for Use/Sterilization

I-125 Seeds are radioactive and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel, consistent with published exposure limits.[2]

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body and, for handling, a ring badge will provide adequate detection.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121° C at 15 psi to 138° C at 35 psi. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138° C and 35 psi).

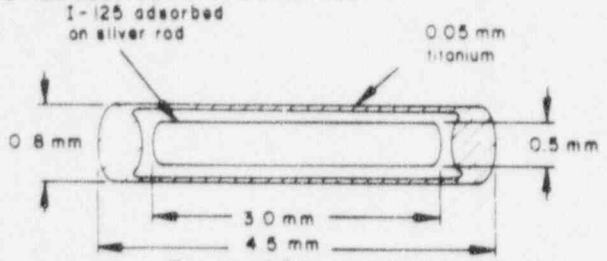
I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and teflon. I-125 Seeds may also be autoclaved in selected accessories to commerically-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun, and nylon and teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion, or inhalation of Iodine-125.

I-125 Seeds
No. 6711

Description

I-125 Seeds 6711 consist of a welded titanium capsule containing iodine-125 adsorbed onto a silver rod.



Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic x-rays and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal radiation emissions are x-rays of 27.4 keV and 35.5 keV.

To correct for the physical decay of iodine-125, the decay factors at selected days after the assay date are shown in the table below.

Decay Chart Iodine-125, Half Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
0	1.000	36	0.661
2	0.977	38	0.646
4	0.955	40	0.631
6	0.933	42	0.617
8	0.912	44	0.603
10	0.891	46	0.589
12	0.871	48	0.575
14	0.851	50	0.562
16	0.832	52	0.550
18	0.813	54	0.537
20	0.794	56	0.525
22	0.776	58	0.513
24	0.759	60	0.501
26	0.741	62	0.490
28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit x-rays of 27.4 and 35.5 keV. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility, and together with the silver rod, results in a total self-absorption of approximately 35%.

Indications

I-125 Seeds with apparent activities from 0.1 to 1.0 mCi are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, slow growth rate, and low to moderate radiosensitivity. Seeds in this apparent activity range may be used to treat superficial, intraabdominal, and intrathoracic tumors. Tumors of the head, neck, lung, pancreas, and prostate (early stages) are commonly treated.

I-125 Seeds with total apparent activities greater than 1.0 mCi are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, and moderate radiosensitivity. These seeds may be used for selected radiation applications as removable implants.

I-125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (e.g. ulcerated) is not recommended with I-125 Seeds.[1]

Warnings

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

Precautions

Preparation for Use/Sterilization

I-125 Seeds are radioactive, and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel consistent with published exposure limits.[2]

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body and, for handling, a ring badge will provide adequate monitoring.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121° C at 15 psi to 138° C at 35 psi. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138° C and 35 psi).

I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and Teflon. I-125 Seeds may also be autoclaved in selected accessories to commerically-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun and nylon and Teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures, or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container, and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion, or inhalation of Iodine-125.

I-125 Seeds In Carrier

M.N. 6720

Description

I-125 Seeds in Carrier consists of a group of I-125 Seeds (up to 20) housed at a fixed distance (0.5 to 1.5 cm center to center) within a braided, synthetic, absorbable carrier. The I-125 Seeds consist of a welded titanium capsule containing iodine-125 absorbed onto either anion exchange resin spheres or a silver rod. The carrier material housing the I-125 Seed is a synthetic absorbable suture material, #1 Vicryl® (polyglactin 910). Seeds are spaced at the distal 2 to 30 cm of the carrier, from which the core has been removed. A surgical needle is attached to the opposite end.

Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic photons and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal photon emissions are 27.4 and 31.4 keV X-rays and a 35.5 keV gamma.

To correct for the physical decay of the Iodine-125, the decay factors at selected days after the assay date are shown in table below.

Decay Chart Iodine-125, Half-Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
	1.000	36	0.661
–	0.977	38	0.646
4	0.955	40	0.631
6	0.933	42	0.617
8	0.912	44	0.603
10	0.891	46	0.589
12	0.871	48	0.575
14	0.851	50	0.562
16	0.832	52	0.550
18	0.813	54	0.537
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28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit 27.4 and 31.4 keV X-rays and a 35.5 keV gamma. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

The dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Intramuscular implantation studied in rats show that the absorption of the carrier in I-125 Seeds in Carrier is minimal until about the 40th postoperative day. Absorption is essentially complete between the 60th and 90th day.

Indications

I-125 Seeds in Carrier is indicated for permanent interstitial implantation of selected tumors which are localized, either unresectable or residual after excision of the primary lesion, and of low to moderate radiosensitivity.[1, 2, 3]

I-125 Seeds in Carrier may be indicated for use concurrent with or at the completion of other treatment modalities, such as external beam radiation therapy or chemotherapy.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (e.g. ulcerated) is not recommended with I-125 Seeds in Absorbable Carrier.

Warnings

I-125 Seeds in Carrier is shipped sterile and must not be resterilized.

Precautions

Preparation for Use

I-125 Seeds in Carrier is radioactive, and appropriate precautions must be taken when handling these devices. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel consistent with published exposure limits.[4]

Personnel monitoring is required for individuals working with I-125 Seeds in Carrier. A film badge or TLD dosimeter worn on the body and, for handling, a ring badge will provide adequate monitoring.

Sterile I-125 Seeds in Carrier is contained within a stainless steel shielding ring. This ring is provided in a moisture-resistant foil pouch within a gas permeable bag. The shielding ring effectively attenuates all radioactivity, eliminating the need for additional shielding.

All manipulations involving I-125 Seeds in Carrier should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds in Carrier should be handled only with forceps, with as much distance as practical between sources and the operator. Spacing of seeds may be adjusted using forceps to manipulate the seeds within the carrier. When using forceps, care must be taken not to crush the seeds.

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures, or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container, and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion, or inhalation of Iodine-125.

Application to Patient

I-125 Seeds in Carrier should be used only by individuals who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and

I-125 Seeds[R]

Certification Sheet

Revised 12/17/82

Medical Products Division/3M

TCAAP
New Brighton, Minnesota 55112

3M

Certification	70-4.9
Iodine-125 Sealed Sources For Medical Uses	1 Sept 1982

Consignee: _____

Address: _____

The following radioactive sources are certified by Minnesota Mining and Manufacturing Company (3M) to have been subjected to the tests described below and to have been given the results listed.

Model Number						
Lot Number						
Quantity						
Activity Range (mCi)*						
Total Activity (mCi)*						
Assay Date						

All seeds have passed an x-ray inspection test and have passed a leak test showing < 0.005 μCi of removable ^{125}Iodine activity. No other certification is to be implied.

* By "mCi" we mean "apparent activity in millicuries", descriptive of output activity only and not the actual millicuries of I-125 contained within the titanium capsule of the I-125 Seed. The actual millicuries of I-125 in Seed Models No. 6701 and 6702 is about (1.19) (apparent activity in mCi) and in Model No. 6711, about (1.54) (apparent activity in mCi).

See the reverse side of this form for information about Seed construction, method of calibration and definition of "apparent activity in millicuries".

Quality Control Date

13567

Medical Products Division/3M

3M Center
St. Paul, Minnesota 55101
612/733 1110

2552

November 26, 1980

Joseph Del Medico
U.S. Nuclear Regulatory Commission
Division of Fuel Cycle and Material Safety
Washington, D.C. 20555

Re: Control No. 02783

Dear Mr. Del Medico:

This is in response to your letter of July 25, 1980, regarding package inserts for I-125 Seeds. Specifically, this submission provides copies of the package inserts for models 6701, 6702, and 6711, which we have revised and reprinted, as agreed to in my letters dated June 3 and 16, 1980, and our telephone conversation of July 9, 1980.

The package inserts for I-125 Seeds contain the following three changes from those texts previously submitted.

1. In the PRECAUTIONS section, addition of the following text as paragraph 7 under 'Preparation for Use/ Sterilization'.

   I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and teflon. I-125 Seeds may also be autoclaved in selected accessories to commercially-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun, and nylon and teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

2. In the first paragraph in the LICENSING section, addition of the symbol, R, following 'I-125 Seeds, to indicate that the phrase is a registered trademark and, hence, the product distributed only by 3M.

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3. In the first paragraph in the LICENSING section, revision of the phrase 'Group IV of 10 CFR Part 35' (incorrectly printed in the original inserts) to 'Group VI of 10 CFR Part 35'.

If you have any questions pertaining to this submission, please feel free to contact me (612/733-6421).

Sincerely yours,

Jacquelyn D. Bush

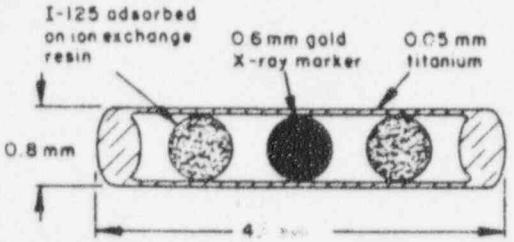
Jacquelyn D. Bush
Sr. Regulatory Compliance Coordinator
Medical Products Division/3M
3M Center, Bldg. 230-3-02
St. Paul, Minnesota 55144

JDB:tmf

I-125 Seeds®
No. 6701

Description

I-125 Seeds 6701 consist of a welded titanium capsule containing Iodine-125 adsorbed on two anion exchange resin spheres. A spherical gold x-ray marker is included, which serves as a means of visualization on radiographs.



Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic x-rays and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal radiation emissions are x-rays of 27.4 keV and 35.5 keV.

To correct for the physical decay of Iodine-125, the decay factors at selected days after the assay date are shown in the table below.

Decay Chart Iodine-125, Half Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
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4	0.955	40	0.531
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18	0.813	54	0.537
20	0.794	56	0.525
22	0.776	58	0.513
24	0.759	60	0.501
26	0.741	62	0.490
28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for Iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit x-rays of 27.4 and 35.5 keV. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility and results in a total self-absorption of approximately 16%.

Indications

I-125 Seeds are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, slow growth rate, and low to moderate radiosensitivity.

I-125 Seeds may be used to treat superficial, intraabdominal or intrathoracic tumors. Tumors of the head, neck, lung, pancreas, and prostate (early stages) are commonly treated.

I-125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (eg, ulcerated) is not recommended with I-125 Seeds.[1]

Warnings

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

Precautions

Preparation for Use/Sterilization

I-125 Seeds are radioactive and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel, consistent with published exposure limits.[2]

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body and, for handling, a ring badge will provide adequate detection.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121° C at 15 psi to 138° C at 35 psi. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138° C and 35 psi).

I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and teflon. I-125 Seeds may also be autoclaved in selected accessories to commercially-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun, and nylon and teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion, or inhalation of Iodine-125.

Application to Patient

I-125 Seeds should be used only by individuals who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.

Radiation detection equipment, capable of detecting 30 keV x-rays, should be available whenever I-125 Seeds are being handled. The seeds are quite small and it may be difficult to locate a dropped seed visually.

All practical physical protection should be provided during the implantation procedure. Frequently, however, protective barriers are not practical in the surgery. In this circumstance, operators must rely upon distance and speed to minimize radiation exposure.[2]

Treatment of Patient

All patients should be informed of the nature of I-125 Seed implants and the expected period of time during which radiation precautions will be necessary. Patients, their close associates, and associated medical personnel should be instructed in the necessary radiation safety procedures required for someone who has received an I-125 Seed implant. Guidelines for necessary precautions have been established by National Council on Radiation Protection and Measurements and are detailed in NCRP Reports.[2, 3, 4, 5, 6]

All patients should be advised of the possibility that, during a course of treatment, one or more I-125 Seeds might slough off and become detached as a tumor regresses and becomes smaller. Under these circumstances, any bandages or linens which come into contact with the site of the implant should be scrutinized for small metallic seeds (¼ of an inch long). Patients should be advised that, whenever seeds are found, they should be picked up with a spoon and placed in a jar or other container, and placed in an inaccessible area in the home. The radiation center should be notified of such an event as soon as possible after its occurrence.

Accountability/Disposal

Iodine-125 is an accountable radioactive material. I-125 Seeds should, therefore, be strictly controlled and stored in a locked safe. If any significant material cannot be accounted for, the loss must be reported to the appropriate federal or state licensing agency.

When disposal is indicated, I-125 Seeds should be transferred to an authorized radioactive waste disposal agency. I-125 Seeds should never be disposed of in normal waste.

An I-125 Seed disposal service is provided by 3M Radiation Therapy Products. Customers wishing to dispose of I-125 Seeds in this manner must contact the 3M Company for approval and specific shipping container and forms.

Material approved for return must comply with Department of Transportation regulations (49 CFR, Parts 171-177) regarding packaging and labeling. Shipments are to be directed to: 3M/Radiation Therapy Products, TCAAP Building 590, New Brighton, Minnesota, 55112.

Leak Testing

NRC regulations (10 CFR 35.14) describe requirements for leak testing radioactive sources.

I-125 Seeds that retain clinical utility for periods of more than six months must be tested at intervals of six months or less as defined in NRC regulations. I-125 Seeds are leak tested prior to shipment and the results are shown on the shipment identification papers that accompany each shipment. I-125 Seeds having a nominal activity of 0.55 mCi comp. will decay in 180 days and will not require leak testing by the user.

Adverse Reactions

No adverse reactions involving I-125 Seeds have been reported.

Dosage and Administration

The total activity of I-125 Seeds required for any given treatment depends upon the tumor volume and the previous radiation history of the tumor site. Established practice[9] should be followed for the calculation of the total activity to be implanted, the proper placement of the sources within the tissue, and the evaluation of the radiation dose distribution achieved.

Dose distribution around each individual seed is not isotropic.[8] This anisotropy should be considered in dose distribution calculations.

Iodine-125 has a 60.2 day half-life. Decay corrections must be made in order to properly calculate the activity of the seeds on the day they are implanted.

Directions for Use

I-125 Seeds will pass through a No. 17 gauge needle. Most implants have been performed with afterloading techniques using an inserter attached to hollow needles. Several devices are available for this purpose. Individual seeds may be implanted using the Scott, Mick and Henschke applicators designed for this purpose. The Royal Marsden Gold Grain gun will not accept I-125 Seeds.

How Supplied

I-125 Seeds are available with an activity per seed of 0.10 to 1.00 mCi comp (nominal 0.55 mCi comp.). The product is supplied as a group of seeds with an assay within a stated range on the assay date. I-125 Seeds with an activity to 40 mCi comp. are available upon special request for use as calibration check sources.

I-125 Seeds are packaged in a screw-cap, 1-dram glass vial, which is labeled to indicate the isotope, amount of activity, activity range and the assay date. Any discrepancy between the number of seeds listed on the certification sheet accompanying the order and the number contained in the vial(s) should be reported to 3M within 24 hours of receipt of the shipment. The vial is contained in a lead pig which is labeled to provide the same information, as well as the number of seeds therein and precautionary regulatory statements pertaining to licensing of the product.

I-125 Seeds are NOT sterile when shipped.

Licensing

I-125 Seeds are licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to §§ 35.14 and 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States.

Federal law restricts this device to sale by or on the order of a physician.

References

1. Hilaris, BS, ed. *Handbook of Interstitial Brachytherapy*. Publishing Sciences Group, Inc., Action, MA, 1975
2. NCRP Report No. 37. NCRP Publication, P.O. Box 30175, Washington, DC 20014
3. NCRP Report No. 40. NCRP Publication, P.O. Box 30175, Washington, DC 20014
4. NCRP Report No. 41. NCRP Publication, P.O. Box 30175, Washington, DC 20014
5. NCRP Report No. 48. NCRP Publication, P.O. Box 30175, Washington, DC 20014
6. NCRP Report No. 49. NCRP Publication, P.O. Box 30175, Washington, DC 20014
7. Scallon, et al. Permanent interstitial therapy using low energy and long half-life radiation sources. *American Journal of Roentgenology*. 105:1 (1969), 157-164
8. Ling, C *Proceedings of Fourth International Conference on Medical Physics*. Ottawa, Canada, July, 1976
9. Anderson, LL Dosimetry with I-125. To be published. Presented at International Endocurietherapy Meeting. LAC/USC, Los Angeles, June 30 - July 2, 1978

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Medical Products Division/3M
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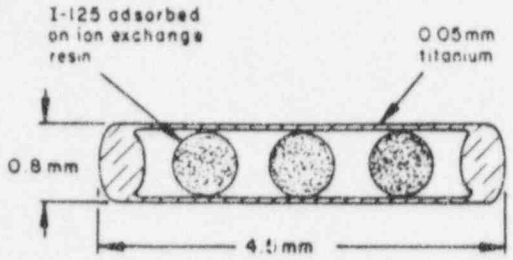
St. Paul, MN 55144

3M

I-125 Seeds®
No. 6702

Description

I-125 Seeds 6702 consist of a welded titanium capsule containing Iodine-125 adsorbed on anion exchange resin spheres.



Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic x-rays and Auger electrons. The electrons are absorbed by the titanium wall of the of the I-125 Seed. The principal radiation emissions are x-rays of 27.4 keV and 35.5 keV.

To correct for the physical decay of Iodine-125, the decay factors at selected days after the assay date are shown in the table below.

Decay Chart Iodine-125, Half Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
0	1.000	36	0.661
2	0.977	38	0.646
4	0.955	40	0.631
6	0.933	42	0.617
8	0.912	44	0.603
10	0.891	46	0.589
12	0.871	48	0.575
14	0.851	50	0.562
16	0.832	52	0.550
18	0.813	54	0.537
20	0.794	56	0.525
22	0.776	58	0.513
24	0.759	60	0.501
26	0.741	62	0.490
28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for Iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit x-rays of 27.4 and 35.5 keV. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility and results in a total self-absorption of approximately 16%.

Indications

I-125 Seeds are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, and moderate radiosensitivity.

I-125 Seeds may be used for selected radiation applications as removable implants.

I-125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (eg, ulcerated) is not recommended with I-125 Seeds.[1]

Warnings

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

Precautions

Preparation for Use/Sterilization

I-125 Seeds are radioactive and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel, consistent with published exposure limits.[2]

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body and, for handling, a ring badge will provide adequate detection.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121° C at 15 psi to 138° C at 35 psi. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138° C and 35 psi).

I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and teflon. I-125 Seeds may also be autoclaved in selected accessories to commerically-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun, and nylon and teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion, or inhalation of Iodine-125.

Application to Pa[illegible]

I-125 Seeds should be used only by indiv[illegible]als who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.

Radiation detection equipment, capable of detecting 30 keV x-rays, should be available whenever I-125 Seeds are being handled. The seeds are quite small and it may be difficult to locate a dropped seed visually.

All practical physical protection should be provided during the implantation procedure. Frequently, however, protective barriers are not practical in the surgery. In this circumstance, operators must rely upon distance and speed to minimize radiation exposure.[2]

Treatment of Patient

All patients should be informed of the nature of I-125 Seed implants and the expected period of time during which radiation precautions will be necessary. Patients, their close associates and associated medical personnel should be instructed in the necessary radiation safety procedures required for someone who has received an I-125 Seed implant. Guidelines for necessary precautions have been established by National Council on Radiation Protection and Measurements and are detailed in NCRP Reports.[2, 3, 4, 5, 6]

All patients should be advised of the possibility that, during a course of treatment, one or more I-125 Seeds might slough off and become detached as a tumor regresses and becomes smaller. Under these circumstances, any bandages or linens which come into contact with the site of the implant should be scrutinized for small metallic seeds (¼ of an inch long). Patients should be advised that whenever seeds are found, they should be picked up with a spoon and placed in a jar or other container, and placed in an inaccessible area in the home. The radiation center should be notified of such an event as soon as possible after its occurrence.

Accountability/Disposal

Iodine-125 is an accountable radioactive material. I-125 Seeds should, therefore, be strictly controlled and stored in a locked safe. If any significant material cannot be accounted for, the loss must be reported to the appropriate federal or state licensing agency.

When disposal is indicated, I-125 Seeds should be transferred to an authorized radioactive waste disposal agency. I-125 Seeds should never be disposed of in normal waste.

An I-125 Seed disposal service is provided by 3M Radiation Therapy Products. Customers wishing to dispose of I-125 Seeds in this manner must contact the 3M Company for approval and specific shipping container and forms.

Material approved for return must comply with Department of Transportation regulations (49 CFR, Parts 171-177) regarding packaging and labeling. Shipments are to be directed to: 3M/Radiation Therapy Products, TCAAP Building 590, New Brighton, Minnesota, 55112.

Leak Testing

NRC regulations (10 CFR 35.14) describe requirements for leak testing radioactive sources.

I-125 Seeds that retain clinical utility for periods of more than six months must be tested at intervals of six months or less as defined in NRC regulations. I-125 Seeds are leak tested prior to shipment and the results are shown on the shipment identification papers that accompany each shipment.

Adverse Reactions

No adverse reactions involving I-125 Seeds have been reported.

Dosage and A[illegible]inistration

The total activity of [illegible]25 Seeds required for any given treatment depends upon the tumor volume and the previous radiation history of the tumor site. Established practice[3] should be followed for the calculation of the total activity to be implanted, the proper placement of the sources within the tissue, and the evaluation of the radiation dose distribution achieved.

Dose distribution around each individual seed is not isotropic.[8] This anisotropy should be considered in dose distribution calculations.

Iodine-125 has a 60.2 day half-life. Decay corrections must be made in order to properly calculate the activity of the seeds on the day they are implanted.

Directions for Use

I-125 Seeds will pass through a No. 17 gauge needle. Most implants have been performed with afterloading techniques using an inserter attached to hollow needles.

How Supplied

I-125 Seeds are available with an activity per seed of 0.10 to 40 mCi comp. The product is supplied as a group of seeds with an assay within a stated range on the assay date.

I-125 Seeds are packaged in a screw-cap, 1-dram glass vial, which is labeled to indicate the isotope, amount of activity, activity range and the assay date. Any discrepancy between the number of seeds listed on the certification sheet accompanying the order and the number contained in the vial(s) should be reported to 3M within 24 hours of receipt of the shipment. The vial is contained in a lead pig which is labeled to provide the same information, as well as the number of seeds therein and precautionary regulatory statements pertaining to licensing of the product.

I-125 Seeds are NOT sterile when shipped.

Licensing

I-125 Seeds are licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to §§ 35.14 and 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States.

Federal law restricts this device to sale by or on the order of a physician.

References

1. Hilaris, BS, ed. *Handbook of Interstitial Brachytherapy*. Publishing Sciences Group, Inc., Acton, MA, 1975
2. NCRP Report No. 37. NCRP Publication, P.O. Box 30175, Washington, DC 20014
3. NCRP Report No. 40. NCRP Publication, P.O. Box 30175, Washington, DC 20014
4. NCRP Report No. 41. NCRP Publication, P.O. Box 30175, Washington, DC 20014
5. NCRP Report No. 48. NCRP Publication, P.O. Box 30175, Washington, DC 20014
6. NCRP Report No. 49. NCRP Publication, P.O. Box 30175, Washington, DC 20014
7. Scallon, et al, Permanent interstitial therapy using low energy and long half-life radiation sources. *American Journal of Roentgenology*. 105:1 (1969), 157-164
8. Ling, C *Proceedings of Fourth International Conference on Medical Physics*. Ottawa, Canada, July, 1976
9. Anderson, LL Dosimetry with I-125. To be published. Presented at International Endocurietherapy Meeting. LAC/USC, Los Angeles, June 30 - July 2, 1978

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St. Paul, MN 55144

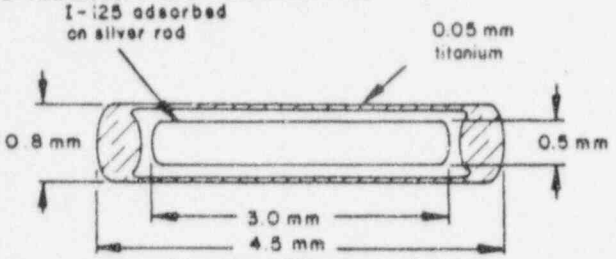
3M

I-125 Seeds®
No. 6711

2552

Description

I-125 Seeds 6711 consist of a welded titanium capsule containing iodine-125 adsorbed onto a silver rod.



Physical Characteristics

Iodine-125 has a half-life of 60.2 days and decays by electron capture with the emission of characteristic x-rays and Auger electrons. The electrons are absorbed by the titanium wall of the I-125 Seed. The principal radiation emissions are x-rays of 27.4 keV and 35.5 keV.

To correct for the physical decay of Iodine-125, the decay factors at selected days after the assay date are shown in the table below.

Decay Chart Iodine-125, Half Life 60.2 Days

Days	Decay Factor	Days	Decay Factor
0	1.000	36	0.661
2	0.977	38	0.646
4	0.955	40	0.631
6	0.933	42	0.617
8	0.912	44	0.603
10	0.891	46	0.589
12	0.871	48	0.575
14	0.851	50	0.562
16	0.832	52	0.550
18	0.813	54	0.537
20	0.794	56	0.525
22	0.776	58	0.513
24	0.759	60	0.501
26	0.741	62	0.490
28	0.724	64	0.479
30	0.708	66	0.468
32	0.692	68	0.457
34	0.676	70	0.447

Radiation Protection

The half value thickness of lead for iodine-125 is 0.025 mm. Thus, a 0.25 mm lead sheet will provide > 99% reduction in exposure.

Actions

I-125 Seeds emit x-rays of 27.4 and 35.5 keV. The clinical efficacy of the sources derives solely from the interaction of these ionizing radiations with the tissue being treated.

Dose distribution around each individual seed is not isotropic. This anisotropy should be included in dose distribution calculations.

Titanium encapsulation assures good tissue compatibility, and together with the silver rod, results in a total self-absorption of approximately 35%.

Indications

I-125 Seeds with activities from 0.1 to 1.0 mCi comp. are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, slow growth rate, and low to moderate radiosensitivity. Seeds in this activity range may be used to treat superficial, intraabdominal, and intrathoracic tumors. Tumors of the head, neck, lung, pancreas, and prostate (early stages) are commonly treated.

I-125 Seeds with activities greater than 1.0 mCi comp. are indicated for interstitial treatment of tumors which have the following characteristics: unresectable, localized, and moderate radiosensitivity. These seeds may be used for selected radiation applications as removable implants.

I-125 Seeds are indicated to treat residual tumors following completion of a course of external radiation therapy. In addition, recurrent tumors may be implanted with I-125 Seeds.

Contraindications

As with other brachytherapy sources, treatment of tumors in generally poor condition (e.g. ulcerated) is not recommended with I-125 Seeds.[1]

Warnings

The I-125 Seed titanium capsule has excellent corrosion resistance, but it is attacked by concentrated hydrochloric acid. I-125 Seeds have been designed not to be used in a concentrated HCl environment.

Precautions

Preparation for Use/Sterilization

I-125 Seeds are radioactive, and appropriate precautions must be taken when handling these sources. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel consistent with published exposure limits.[2]

Personnel monitoring is required for individuals working with I-125 Seeds. A film badge or TLD dosimeter worn on the body and, for handling, a ring badge will provide adequate monitoring.

I-125 Seeds are provided in a glass vial which should be maintained in a lead vial container for storage. When transporting seeds within the hospital premises, an appropriate carrier with adequate shielding should be used.

All manipulations involving I-125 Seeds should be carried out behind shielding of such size and thickness as will adequately shield the operator. DIRECT CONTACT WITH THE SOURCES SHOULD BE AVOIDED. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. I-125 SEEDS SHOULD NOT BE PICKED UP WITH THE HANDS.

I-125 Seeds are NOT sterile when shipped and as such must be sterilized with steam (autoclave) or ethylene oxide (EO) before implantation. Regardless of the method selected, I-125 Seeds should be placed in an adequately shielded container prior to placement in the sterilization chamber. Manipulation of the seeds prior to or following sterilization should be carried out behind shielding of such size and thickness as will adequately shield the operator. In addition, I-125 Seeds should be handled only with forceps, with as much distance as practical between sources and the operator. Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.

I-125 Seeds have been designed to withstand normal autoclave temperature and pressure variations from 121° C at 15 psi to 138° C at 35 psi. I-125 SEEDS ARE NOT INTENDED TO BE STERILIZED USING DRY HEAT AND SHOULD NOT BE SUBJECTED TO TEMPERATURES AND PRESSURES IN EXCESS OF THESE LIMITS (138° C and 35 psi).

I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and teflon. I-125 Seeds may also be autoclaved in selected accessories to commerically-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun, and nylon and teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Although I-125 Seeds have a high structural integrity, it is possible, through rough handling, high temperatures, or crushing, that a seed could leak or be ruptured. If such a rare occurrence does happen, the area should be closed off, the seeds packaged into a sealed container, and the area decontaminated. Decontamination can be confirmed by taking "wipe" samples of the immediate area. Personnel movement should be controlled to avoid spread of any radioactive contamination. Whenever a source is damaged, personnel working in the area should undergo a thyroid scan to assure that they have not been contaminated by contact, ingestion, or inhalation of Iodine-125.

Application to Pa[illegible]

I-125 Seeds should be used only by individuals who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.

Radiation detection equipment capable of detecting 30 keV x-rays, should be available whenever I-125 Seeds are being handled. The seeds are quite small, and it may be difficult to locate a dropped seed visually.

All practical physical protection should be provided during the implantation procedure. Frequently, however, protective barriers are not practical in the surgery. In this circumstance, operators must rely upon distance and speed to minimize radiation exposure.[2]

Treatment of Patient

All patients should be informed of the nature of I-125 Seed implants and the expected period of time during which radiation precautions will be necessary. Patients, their close associates and associated medical personnel should be instructed in the necessary radiation safety procedures required for someone who has received an I-125 Seed implant. Guidelines for necessary precautions have been established by National Council on Radiation Protection and Measurements and are detailed in NCRP.[2, 3, 4, 5, 6]

All patients should be advised of the possibility that, during a course of treatment, one or more I-125 Seeds might slough off and become detached as a tumor regresses and becomes smaller. Under these circumstances, any bandages or linens which come into contact with the site of the implant should be scrutinized for small metallic seeds (¼ of an inch long). Patients should be advised that whenever seeds are found, they should be picked up with a spoon and placed in a jar or other container, and placed in an inaccessible area in the home. The radiation center should be notified of such an event as soon as possible after its occurrence.

Accountability/Disposal

Iodine-125 is an accountable radioactive material. I-125 Seeds should, therefore, be strictly controlled and stored in a locked safe. If any significant material cannot be accounted for, the loss must be reported to the federal or state licensing agency.

When disposal is indicated, I-125 Seeds should be transferred to an authorized radioactive waste disposal agency. I-125 Seeds should never be disposed of in normal waste.

An I-125 Seed disposal service is provided by 3M Radiation Therapy Products. Customers wishing to dispose of I-125 Seeds in this manner must contact the 3M Company for approval and specific shipping container and forms.

Material approved for return must comply with Department of Transportation regulations (49 CFR Parts 171-177) regarding packaging and labeling. Shipments are to be directed to: 3M/Radiation Therapy Products, TCAAP Building 590, New Brighton, Minnesota, 55112.

Leak Testing

NRC regulations (10 CFR 35.14) describe requirements for leak testing radioactive sources.

I-125 Seeds that retain clinical utility for periods of more than six months must be leak tested at intervals of six months or less as defined in NRC regulations.

I-125 Seeds are leak tested prior to shipment and the results are shown on the shipment identification papers that accompany each shipment. I-125 Seeds having a nominal activity of 0.55 mCi comp. will decay to 0.07 mCi in 180 days and will not require leak testing by the user.

Adverse Reactions

No adverse reactions involving I-125 Seeds have been reported.

Dosage and A[illegible]nistration

The total activity of I-125 Seeds required for any given treatment depends upon the tumor volume and the previous radiation history of the tumor site. Established practice[9] should be followed for the calculation of the total activity to be implanted, the proper placement of the sources within the tissue, and the evaluation of the radiation dose distribution achieved.

Dose distribution around each individual seed is not isotropic.[8] This anisotropy should be included in dose distribution calculations.

Iodine-125 has a 60.2 day half-life. Decay corrections must be made in order to properly calculate the activity of the seeds on the day they are implanted.

Directions for Use

I-125 Seeds will pass through a No. 17 gauge needle. Most implants have been performed with afterloading techniques using an inserter attached to hollow needles. Several devices are manufactured for this purpose. Individual seeds may be implanted using the Scott, Mick, and Henschke applicators designed for this purpose. The Royal Marsden Gold Grain gun will not accept I-125 Seeds.

How Supplied

I-125 Seeds, model 6711, are available with an activity per seed of 0.10 to 40 mCi comp. The product is supplied as a group of seeds with an assay within a stated range on the assay date.

I-125 Seeds are packaged in a screw-cap, 1-dram glass vial, which is labeled to indicate the isotope, amount of activity, activity range, and the assay date. Any discrepancy between the number of seeds listed on the certification sheet accompanying the order and the number contained in the vial(s) should be reported to 3M within 24 hours of receipt of the shipment. The vial is contained in a lead pig which is labeled to provide the same information, as well as the number of seeds therein and precautionary regulatory statements pertaining to licensing of the product.

I-125 Seeds are NOT sterile when shipped.

Licensing

I-125 Seeds are licensed by the U.S. Nuclear Regulatory Commission for distribution to persons licensed pursuant to §§ 35.14 and 35.100 Group VI of 10 CFR Part 35 or under equivalent licenses of Agreement States.

Federal law restricts this device to sale by or on the order of a physician.

References

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2. NCRP Report No. 37. NCRP Publications, P.O. Box 30175, Washington, D.C., 20014.
3. NCRP Report No. 40. NCRP Publications, P.O. Box 30175, Washington, D.C., 20014.
4. NCRP Report No. 41. NCRP Publications, P.O. Box 30175, Washington, D.C., 20014.
5. NCRP Report No. 48. NCRP Publications, P.O. Box 30175, Washington, D.C., 20014.
6. NCRP Report No. 49. NCRP Publications, P.O. Box 30175, Washington, D.C., 20014.
7. Scallon, et al. *American Journal of Roentgenology*. Vol. 105. No. 1 (1969). pp. 157-164.
8. Ling, Cliff. *Proceedings of Fourth International Conference on Medical Physics*. Ottawa, [illegible]. July, 1976.
9. Anderson, L.L. To be published. Presented at International Endocurietherapy Meeting, LAC/USC, Los Angeles, 6/30/78-7/2/78.

7-80

Medical Products Division/3M
225-5S 3M Center
St. Paul, MN 55144

3M

Medical Products Division/3M

3M Center
St. Paul, Minnesota 55101
612/733 1110

June 3, 1980

3M

U. S. Nuclear Regulatory Commission
NMSS
Materials Certification and Procedures Branch
Washington, D.C. 20555
Attention: Earl G. Wright

Re: Materials License No. 22-00057-59MD, Amendment No. 02
3M Submissions to NRC dated February 8, 1980; April 18, 1980; and May 8, 1980

Dear Mr. Wright:

This letter is in response to our telephone conversation of yesterday, during which we discussed the sterilization conditions for I-125 Seeds® and other concerns pertaining to seed construction. Specifically, this submission provides additional information in support of our pending license amendment application for distribution of the model 6711 I-125 Seed.

In an effort to prevent the reoccurrence of a recent misuse incident involving I-125 Seeds, 3M is preparing to revise the package insert for the model 6711 seed, as we agreed during our discussion. The following text will be added to the PRECAUTIONS section, as paragraph 7 under 'Preparation for Use/Sterilization" (page 25 of the February 8 submission).

> I-125 Seeds should be autoclaved in bulk or individually in appropriate containers of autoclave-compatible materials. These materials include stainless steel, glass, nylon, and teflon. I-125 Seeds may also be autoclaved in selected accessories to commercially-available implant tools. Among these accessories are the stainless steel cartridge of the Mick applicator and gun, and nylon and teflon tubing used as seed holders with Henschke and Scott applicators. When in doubt about the chemical nature of these seed holders, either sterilize the materials with ethylene oxide or autoclave a sample of the materials containing dummy seeds before attempting to load with radioactive seeds. DO NOT AUTOCLAVE I-125 SEEDS IN PLASTIC TUBING OR OTHER PLASTIC CONTAINERS.

Similarly, this text will be added to the existing package inserts for I-125 Seeds, models 6701 and 6702, currently being distributed.

As you requested, I am enclosing from our files copies of instructions for use of the Mick I-125 Gun, Mick Applicator, and Henschke Applicator. In addition, a reprint of an article entitled Rapid Injector for Permanent Radioactive Implantation describes generally the use of the Scott applicator,

We would appreciate your expeditious review of this submission. If you have any questions regarding information presented herein, please feel free to contact me (612/733-6421).

Sincerely yours,

Jacquelyn D. Bush

Jacquelyn D. Bush
Sr. Regulatory Compliance Coordinator
Medical Products Division/3M
3M Center, 230-3
St. Paul, Minnesota 55144

JDB:
Enclosures:5

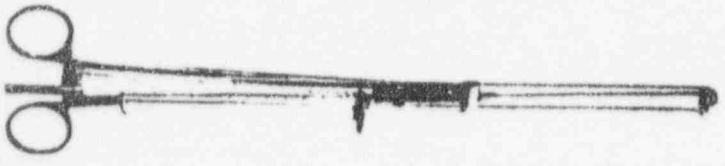
^{125}I PERMANENT IMPLANT INSTRUMENTS

Long experience in the field of permanent interstitial implantation, our personal contact with today's leading radiologists, and our combined technical knowledge, have produced a line of the finest quality instruments, successfully utilized throughout the United States, Canada, Mexico, South America, Europe and the Far East.

All implantation techniques are based on the afterloading principle — needles are inserted into the tumor first and seeds, with the aid of an instrument, accurately placed or spaced in any area. Thus, since seeds are handled at a distance, exposure to hands is reduced.

All our instruments are sold in an attractive wooden case containing a stainless steel tray for sterilisation, and we provide a yearly maintenance program for all our permanent interstitial instruments, keeping them clean, attractive and in excellent operating condition.

HENSCHKE PERMANENT INTERSTITIAL IMPLANT INSTRUMENT #6501



- single seed transfer
- lightweight
- suitable for ^{125}I, ^{222}Rn &
- durable construction
- all stainless steel
- easy cleaning
- rapid exchange of needle
- accurate retraction due to ratched mechanism
- maximum seeds per needle = 12

I-125 GUN #7203

- suitable for all types of implants
- accurate placement of seeds up to 12 cm
- consecutive insertion of seeds
- easy and accurate retraction of needle due to trigger mechanism
- easy exchange of needles
- steady control over instrument due to excellent grip
- rugged construction
- easy cleaning
- minimum exposure due to high density material used in magazine and magazine holder

MICK APPLICATOR #7308

- lightweight
- easy handling due to simplicity of instrument
- quick exchange of needles without removal of magazine
- suitable for single seed or superficial implants
- ideal for implants of the prostate
- fast insertion of seeds
- accurate placement of seeds up to 12 cm
- rugged construction
- easy cleaning

LOADING ACCESSORIES

- #7508 L—BLOCK a protective lightweight barrier with lead glass
- #7509 V—BLOCK for easy loading of cartridges
- #7605 I-125 CARRIER for carrying preloaded nylon tubes in protective chrome-plated container

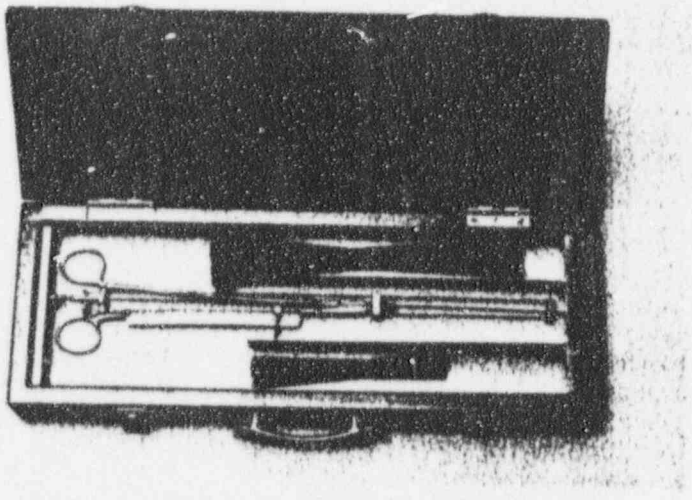
For further information, please write to:

Mick Radio-Nuclear Instruments, Inc.

1470 Outlook Avenue, Bronx, N.Y. 10465
(212) 597-3999

Henschke

Permanent Interstitial Implant Set



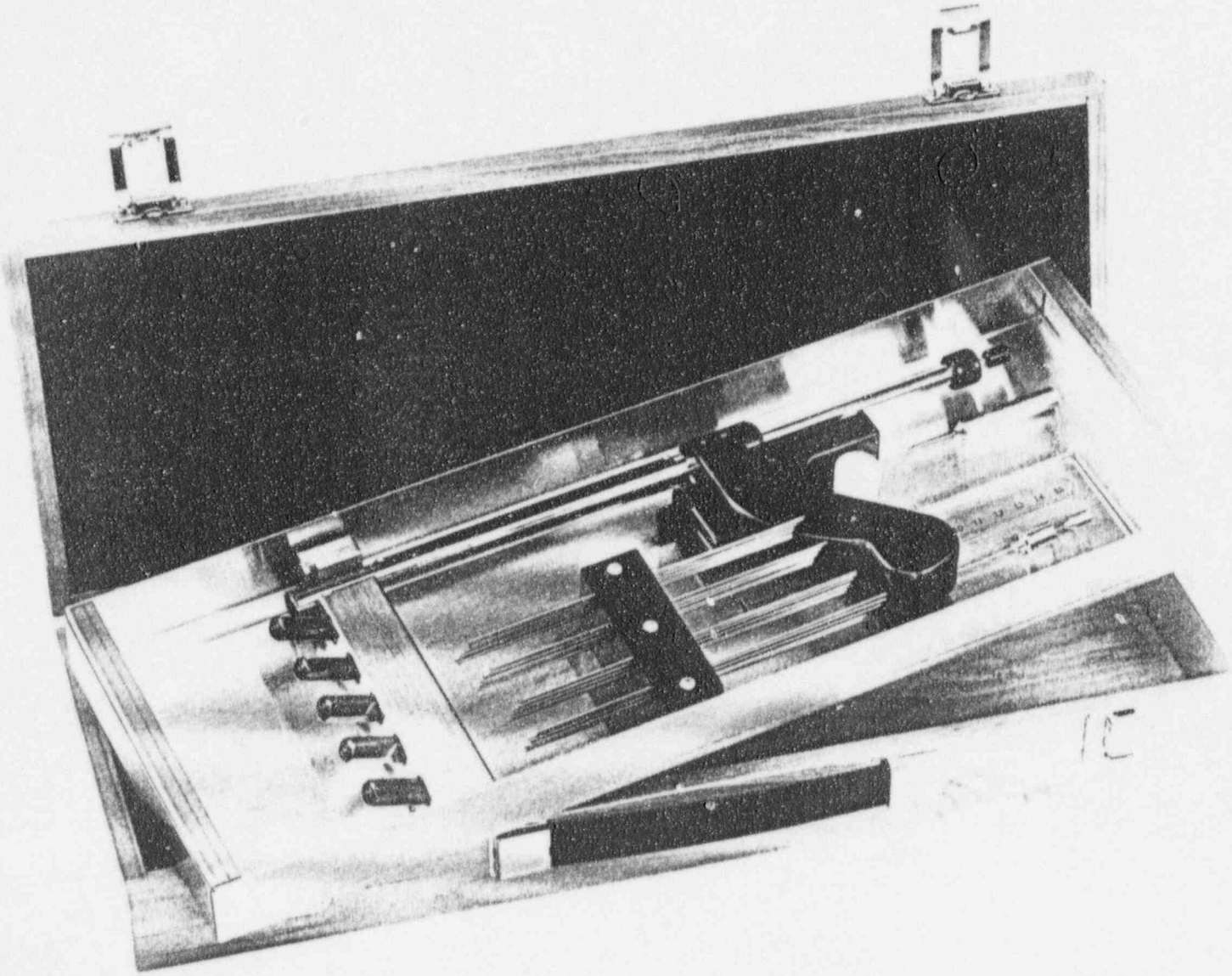
Permanent implants have in the past found their principal indication in palliative cancer treatment. However, with the improved implantation techniques and new radioisotope sources, they are being used more and more for curative therapy as well.

As the first step, unloaded, hollow 17-gauge needles, each 15 cm long, are inserted in and around the tumor. If feasible, the tumor should be so exposed that one hand can be placed under it. By measuring the length of the needles outside the tumor, the shape and size of the implanted volume can be determined. The number of sources required to give the desired dose is then calculated.

As the second step, an instrument with a depth gauge is attached to each needle in turn. Through it the required number of radioisotope sources are introduced one by one into the tissue and implanted at the desired depth.

I-125 GUN

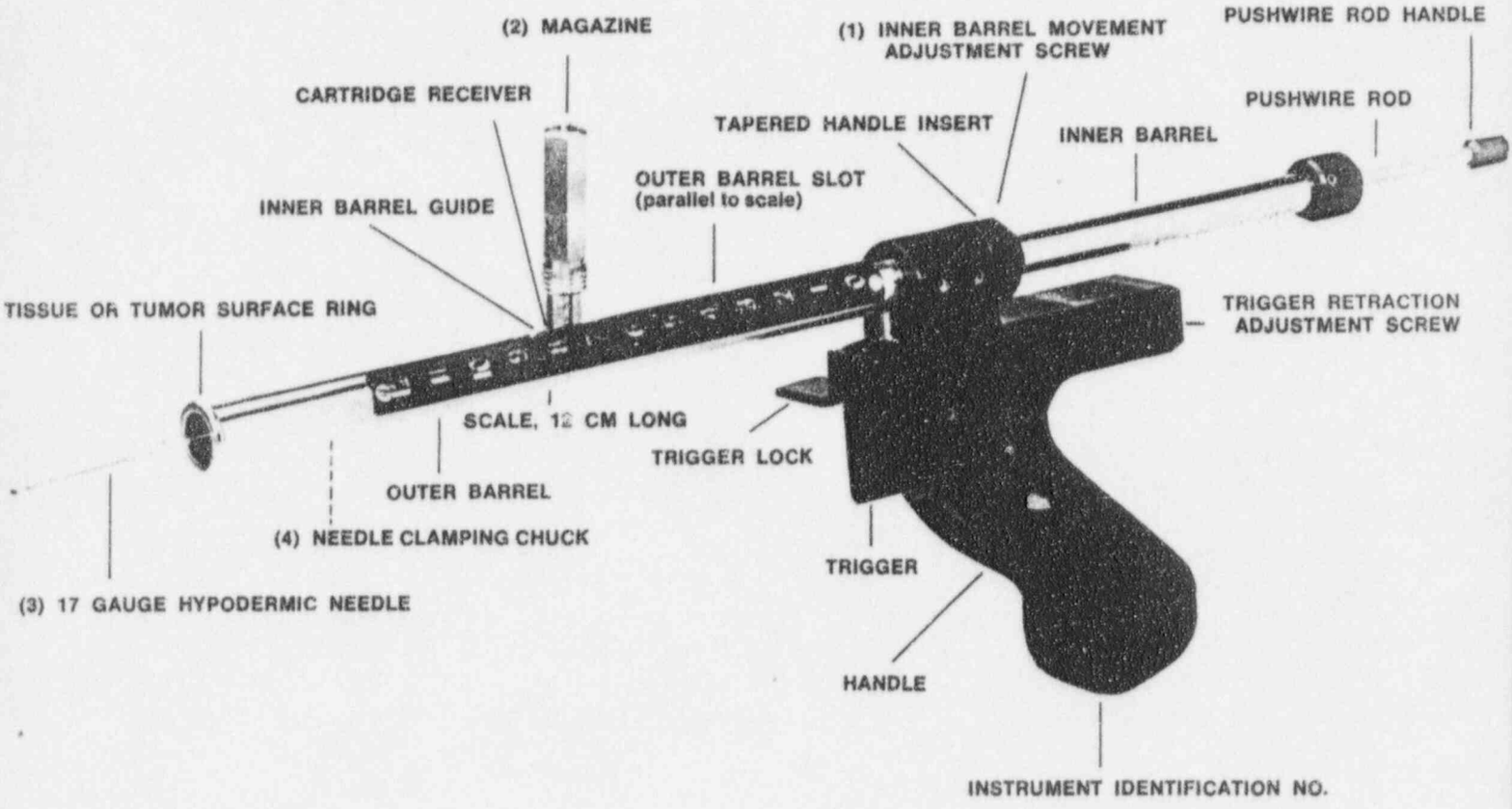
FOR IMPLANTATION OF I-125 SEEDS AND AU-198 GRAINS



Mick Radio-Nuclear Instruments, Inc.

1470 Outlook Avenue, Bronx, N. Y. 10465
(212) 597-3999

DESCRIPTION



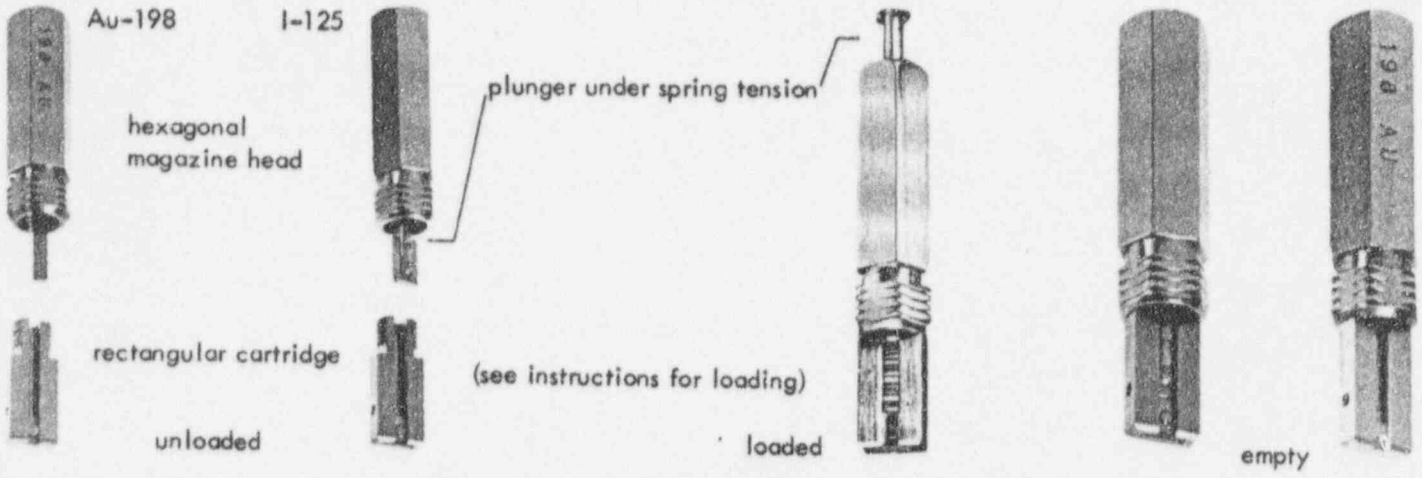
(1) The inner barrel movement can be tightened or loosened by adjusting the set screw located on top of tapered handle insert

(2) See detailed illustration on magazine

(3) 17 gauge, 15 cm long, 45° point stainless steel hypodermic needle

(4) Setting the tissue ring to the tumor surface, the needle clamping chuck disappears in the outer barrel

MAGAZINE



THE I-125 GUN

Development on the I-125 Gun started in 1968 at Memorial Hospital, New York City, by B. Hilaris and D. Mahan and was continued by Felix W. Mick in collaboration with F. Nauroschat.
The I-125 Gun is based on the same afterloading principle as the Henschke Permanent Interstitial Implant Instrument and the Mick Applicator. All instruments are provided with a ratched mechanism assuring accurate placement of seeds at any desired depth up to 12 cm. The needles are withdrawn at 5 mm steps by means of a trigger mechanism and seeds are manually transferred into the tumor with a stylet.

FEATURES

- SUITABLE FOR ALL TYPES OF IMPLANTS USING I-125 SEEDS AND AU-198 GRAINS
- ACCURATE PLACEMENT OF SEEDS UP TO 12 CM
- CONSECUTIVE INSERTION OF SEEDS
- EASY AND ACCURATE RETRACTION OF NEEDLE DUE TO TRIGGER MECHANISM
- EASY EXCHANGE OF NEEDLES
- STEADY CONTROL OVER INSTRUMENT DUE TO EXCELLENT GRIP
- RUGGED CONSTRUCTION
- MINIMUM EXPOSURE DUE TO HIGH DENSITY MATERIAL USED IN MAGAZINE AND MAGAZINE HOLDER
- ALL MATERIAL STAINLESS STEEL OR SURFACE TREATED (AUTOCLAVABLE)
- EASY CLEANING

SET INCLUDES:

7203-1	1-125 Gun
7203-2	magazines (5)
7203-3	hypodermic stainless steel needles (15 cm long, 17 gauge, 45° point) (32)
7203-4	needle holder (1)
7203-5	magazine holder (1)
7203-6	stainless steel lift-out tray for sterilization (1)
7203-7	allenwrench for #6 set screws (1)
7203-8	stainless steel ruler, 15 cm long
7701	obturators (4)
7702	loop wire (1)
7703	needle funnel attachment (1)
7704	L-ruler (1)

INSTRUCTIONS

Modified by P. Veerling

INTRODUCTION

The preparation of the I-125 Gun prior to surgery is most important. Many difficulties and inconveniences will be avoided by carefully following certain steps. As with any other new equipment, it is vital to get acquainted with its features and functions before using in surgery. Particular attention should be given to the details of attaching the guide needles to the applicator to insure proper seating and fit, and to the vertical spacing procedures during implantation of the seeds.

The I-125 Gun is basically a very simple instrument and its construction is rugged enough so that damage during normal use is practically impossible. Naturally, good care must be taken after each use. All parts should be cleaned and stored in their designated locations. The needles should be placed in the needle holder, which contains four slots for eight needles each. The magazine holder is provided with five holes to store five magazines. The instrument can be cleaned by soaking in hydrogen peroxide immediately after use followed by gentle scrubbing with a soft brush and spraying with jets of water. The sterilization tray can be cleaned with a regular stainless steel cleaning spray. After all parts are correctly stored, it is immediately visible if the set is complete.

PREPARATION FOR USE

The stainless steel tray containing the applicator and accessories should be examined for completeness. All parts should be visually examined and any moving parts should be quickly tested for smoothness of motion. The guide needles should be straight, not crimped, and the points should be sharp.

The first step in preparing the instrument for implantation of I-125 seeds is loading of the magazines. The magazines are stored in the magazine holder of the stainless steel tray and may be removed by unscrewing counter-clockwise (clockwise for storage). The magazine consists of two components: magazine head and cartridge. The magazine head is a hexagonal body containing a plunger under spring tension. The cartridge has a rectangular shape and contains a slot to hold the I-125 seeds. The front of the cartridge is open for loading. The cartridge is best loaded using our V-block (see our leaflet for loading accessories). Pick up the seeds with our special forceps and feed it into the slot from top to bottom. It is important that the seed is not dropped into the cavity, but placed carefully at the bottom of the cartridge. The next seed is picked up in the same manner and fed into the slot until it rests parallel on top of the previous one. This procedure is repeated until the cartridge is filled to capacity of ten (10) seeds. The seeds should slide smoothly and fit across the opening in the front of the cartridge. Seeds which are under or oversized should not be used since they could cause jamming of the magazine or applicator. When the cartridge is loaded to capacity, insert the magazine head plunger into the cartridge slot and turn clockwise with slight downward pressure until it stops. The magazine is now ready for implantation and can be put back into the stainless steel tray.

The entire stainless steel tray and its contents may be sterilized by autoclaving just prior to use. The wooden case is used for transportation and shelf storage only.

Magazines for Au-198 grains are available and work with the same principle, except that the receiving slot is smaller to accommodate the size of the grains. Au-198 magazines are easily identified because of their golden color.

AFTERLOADING TECHNIQUE

The implantation of the I-125 seeds is done by means of an after-loading technique. This technique consists of five basic steps: 1) plan distribution of seeds; 2) insert guide needles; 3) attach applicator to needles; 4 insert magazine containing radioactive seeds and, 5) implant seeds through guide needles.

Using the tumor volume and shape, seed strength, and desired therapeutic dose, the spacing between guide needles and between seeds should be planned so as to achieve the desired therapeutic effect with a minimum of complications. The dosimetry of I-125 seed implants is discussed in *Handbook of Interstitial Brachytherapy*, edited by Basil S. Hilaris, M.D. of Memorial Sloan Kettering Cancer Center (published by Publishing Sciences Group, Inc., Acton, Mass. 1975).

Insertion of guide needles may be accomplished as follows: Insert hollow 17 gauge stainless steel needles, 15 cm long, and ground to a 45 degree point, around the periphery of the tumor mass. (For implants through the intact skin, needles with sharp points are preferrable, but for intrathoracic and intro-abdominal implants, it is better to use less sharp needles that do not penetrate and change their position so easily). For a spherical shaped tumor, 0.55 millicurie nominal seed strength and an aim of 16000 rads delivered through total decay, needles are usually spaced 1 cm apart for tumors up to 4 cm in diameter, 1.5 cm apart for tumors from 4 cm to 8 cm, and 2 cm apart for larger tumors. All needles should be inserted parallel to each other. The direction of the needles must be considered carefully before starting, so that their position may be palpated and the maximum number of seeds inserted through one needle. Each guide needle is 15 cm long which means that the length of guide needle implanted within a tumor bed may be calculated once the length of protruding needle is known. This will give a guide as to the number of seeds to be inserted in each needle, once the vertical spacing is also determined.

Attachment of the I-125 Gun to the guide needles may be accomplished as follows: After all needles have been inserted into the tumor to the required depth, remove I-125 Gun from the stainless steel tray and place horizontally in hand. While holding the instrument, with index finger press down trigger lock and with the other hand pull stylet out to its extreme end. Remove protective needle from needle clamping chuck by turning it clockwise. In order to avoid deeper penetration of the guide needle, a hemostat may be clamped to the needle at the tissue surface prior to attaching the applicator to the needle. Next, lower the Gun over the protruding part of the needle and when it has reached a definite stop, turn the needle chuck cap clockwise as far as possible.

With the needle firmly attached to the instrument, a pin located in the needle chuck-cap will appear in the middle of the tissue ring cut-out. Check if needle is firmly atached to the instrument by slightly lifting the instrument upward while grasping the needle firmly. Care must be taken at this point not to displace the correctly inserted needle by pulling it out of the tissue.

To establish the depth of the inserted needle, set the tissue ring to the tumor surface. With index finger of one hand depress trigger lock and with the other hand hold inner barrel steady (behind the instrument handle) and lower Gun to the tumor surface. Release trigger lock and remove hemostat. The rectangular opening (cartridge receiver) appearing through the outer barrel slot indicates the depth of needle on the adjacent scale, where the first seed should be placed.

Insertion of the seed magazine is as follows: the loaded magazine is taken out of storage position and inserted all the way into the rectangular cartridge receiver of the inner barrel with the cartridge slot aiming away from the scale. Note that the stylet must be completely retracted out of position in order to allow the cartridge to be inserted. The magazine is firmly in place once a click is heard indicating that the small ball is caught in the indentation of the magazine.

Implantation of the seeds is accomplished as follows. The first of the ten seeds in the cartridge is deposited into the needle by pushing the stylet all the way down. In order to penetrate hard tissue it may be necessary to apply extra pressure to push the wire rod handle as it reaches its end. If the stylet is not completely depressed, the seed will remain in the needle, thus by inserting the next seed, two seeds will be placed on top of each other. Palpation of the under side of the tumor mass during this process can generally give assurance that the seed has in fact been deposited at the bottom of the needle.

To insert the next seed, usually spaced 1 cm, pull trigger twice (two clicks = 1 cm), three clicks for 1,5 cm. Pull stylet out to its extreme end and observe

To attach the Gun to the following needle, with index finger of one hand depress the trigger lock and with other hand push the inner barrel completely forward. Pull stylet out to its extreme end, turn needle clamping chuck clockwise one half turn, remove needle and lower Gun as far as it will go over protruding part of next needle. (To move the inner barrel the trigger lock must be depressed.)

During the implant procedure, it is recommended that the instrument be rinsed frequently in normal saline or heparin solution in order to remove tissue or blood which will interfere with smooth movement of the moving parts of the applicator. A small syringe or asepto is helpful in forcing the solution through the chuck and magazine receiving areas.

In addition to radiation exposure precautions, an accurate accountability of all sources must be maintained. For this reason, records of sources implanted and remaining sources must coincide with the number of seeds available. All instruments and surgical accessories including sponges and suction devices should be surveyed immediately after the implant procedure. Follow-up of patients may be necessary in order to retrieve sources which are sloughed off post-operatively.

Another danger in use of the applicator for I-125 seeds is the rupture of the outer metal encapsulation. This could occur through excessive use of force in the event of a sticking seed or seed in a cartridge. The tiny ceramic beads containing radioactive I-125 are barely visible once the capsule is ruptured. This can be avoided by proper use of the instrument and sizing of the seeds before use.

An individual familiar with radiation safety procedures and pertinent regulations should be consulted prior to undertaking an implant program in order to assure proper radiation safety of personnel, patient, patient's family, and the general public. A number of guidelines are available through the National Council on Radiation Protection and Measurements, 4201 Connecticut Avenue, NW, Washington, D.C. 20008 and the source suppliers.

CLEANING

Immediately after the implant procedure and before start of the cleaning operations, all guide needles should be checked for possible remaining seeds. This can be accomplished by inserting the loop wire through each needle and observing for any seeds which are ejected from the bottom.

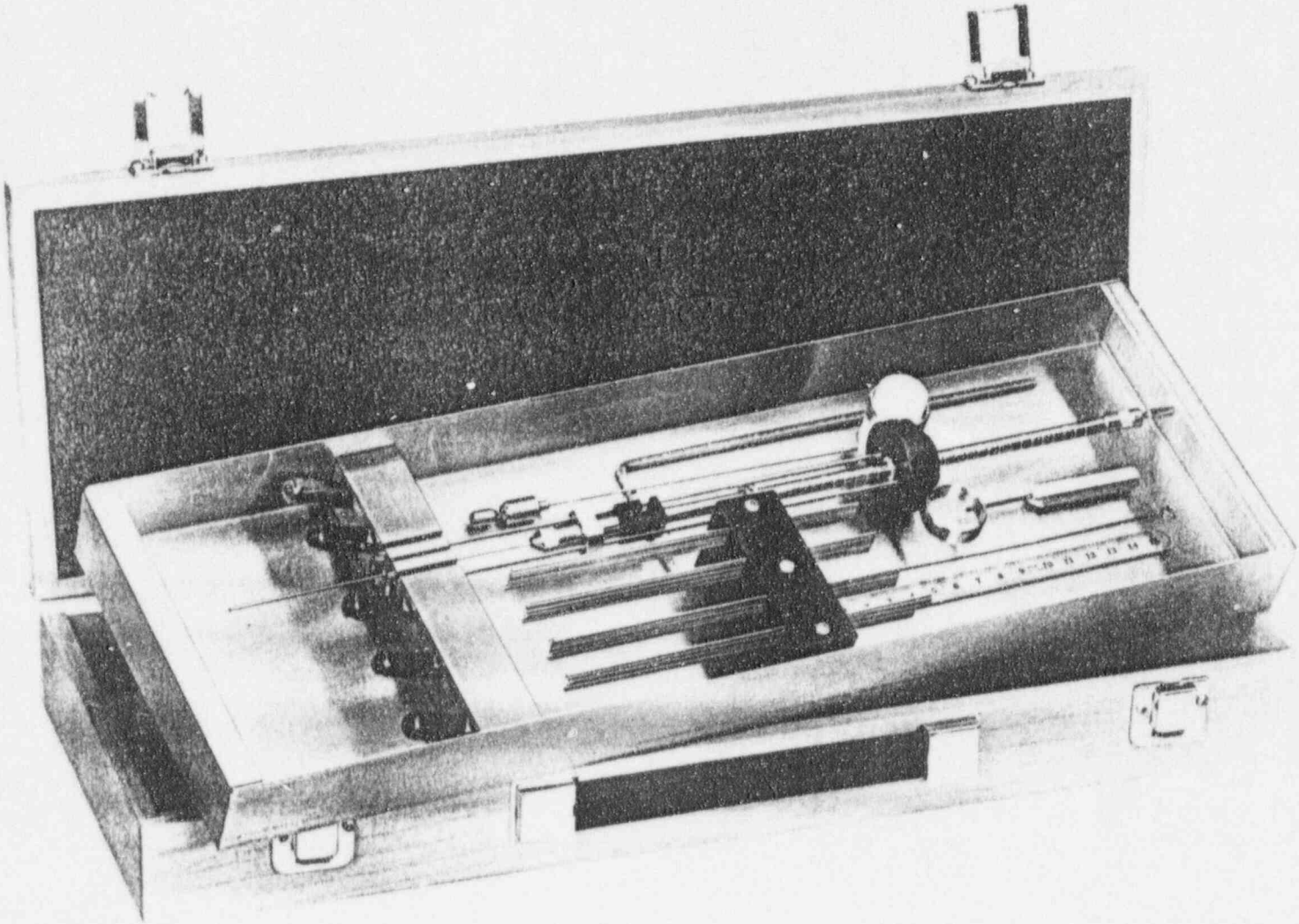
For best results remove tissue and blood from instrument immediately after use. Soaking in hydrogen peroxide or heparin solution should loosen all biological materials. The applicator and accessories should be gently scrubbed with a soft brush and loose materials washed away with a jet of water. A loop wire is included for removing stubborn debris from guide needles. Keeping the instruments clean and in good operating condition insures a precise and efficient implant procedure.

RADIATION SAFETY

Using the I-125 Gun and accessories entails handling solid radioactive sources, namely I-125 seeds, Au-198 grains and similar sources. As with any other sources, the principles of time, distance, and shielding should be utilized. Personnel monitoring devices, such as low energy pocket chambers, film badges and thermoluminescence dosimeter devices, should be utilized. Portable shielding devices for bodies and eyes are available as accessories through this company. Lead-rubber gloves are available for surgical manipulation and handling during the implant procedure. These are especially effective for I-125 seed implants because of the low energy of the radionuclide.

MICK APPLICATOR

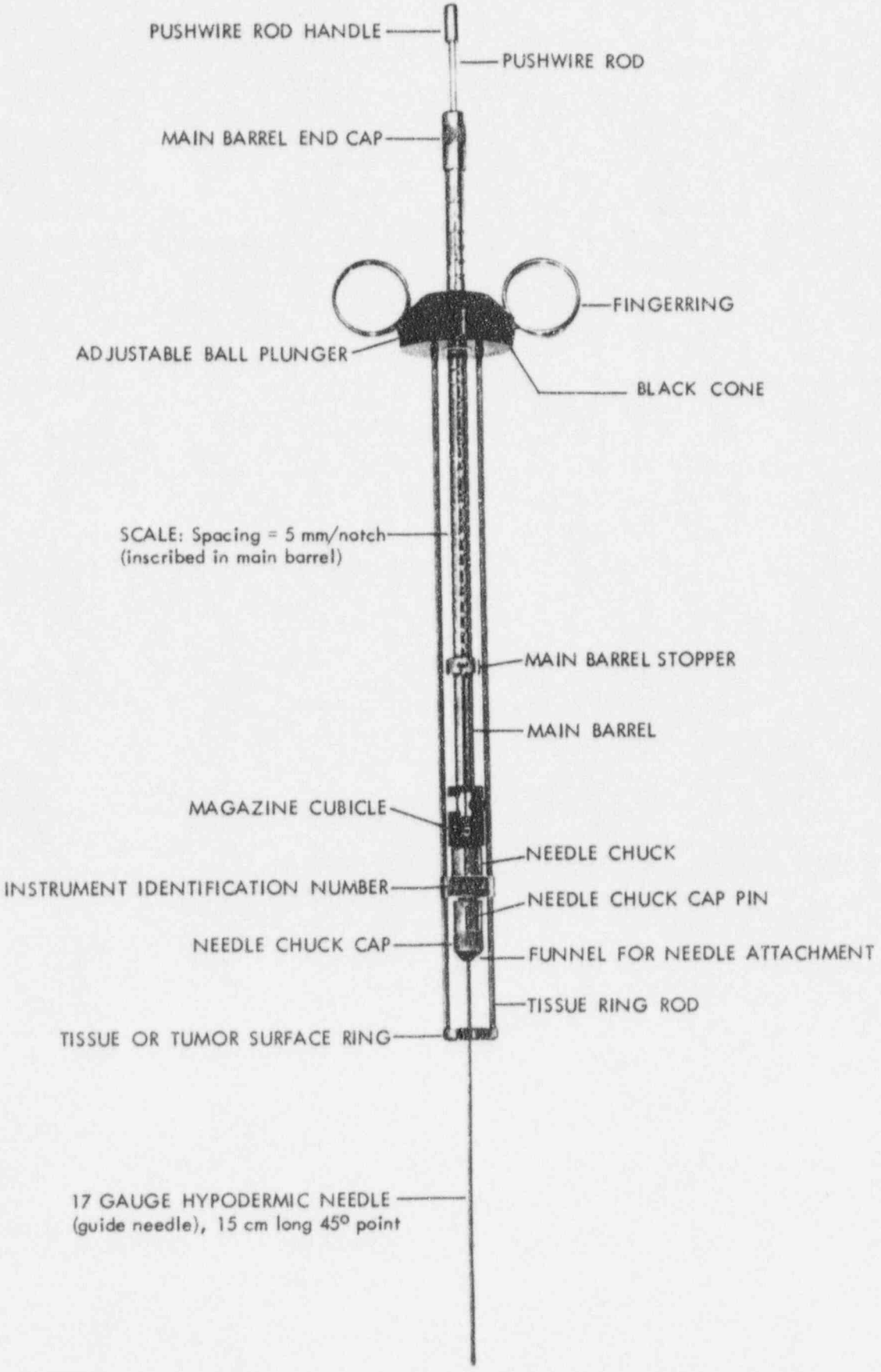
FOR IMPLANTATION OF I-125 SEEDS AND AU-198 GRAINS



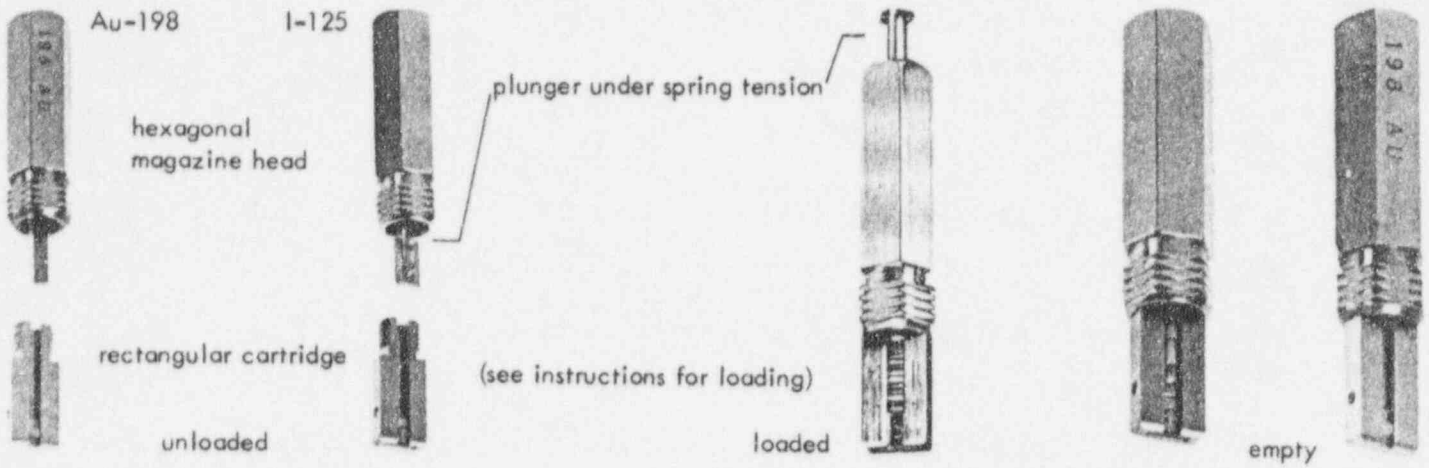
Mick Radio-Nuclear Instruments, Inc.

1470 Outlook Avenue, Bronx, N.Y. 10465
(212) 597-3999

DESCRIPTION



MAGAZINE



THE MICK APPLICATOR

is based on the same afterloading principle as the Henschke Implant Instrument and the I-125 Gun. These instruments are provided with a ratched mechanism assuring accurate placement of seeds at any desired depth up to 12 cm. Needles can be withdrawn at 5 mm steps and seeds are manually transferred by means of a stylet into the tumor.

FEATURES

- lightweight
- easy handling due to simplicity of instrument
- quick exchange of needles without removal of magazine
- suitable for single seed or superficial implants
- ideal for implants of the prostate
- fast insertion of seeds
- accurate placement of seeds up to 12 cm
- minimum exposure due to high density material in magazine
- rugged construction
- all material stainless steel or surface treated
- easy cleaning

SET INCLUDES:

7308	- Mick Applicator
7609	- magazines (5)
7308-3	- hypodermic stainless steel needles (15 cm long)(32)
7610	- stainless steel ruler (1)
7308-5	- needle holder (1)
7308-6	- magazine holder (1)
7701	- obturators (4)
7702	- loop wire (1)
7703	- needle funnel attachment (1)
7704	- stainless steel L-ruler (1)
7308-7	- stainless steel lift-out tray for sterilization (1)
7308-8	- wooden carrying case (1)

INSTRUCTIONS

Modified by P. Veerling

INTRODUCTION

The preparation of the Mick applicator prior to surgery is most important. Many difficulties and inconveniences will be avoided by carefully following certain steps. As with any other new equipment, it is vital to get acquainted with its features and functions before using in surgery. Particular attention should be given to the details of attaching the guide needles to the applicator to insure proper seating and fit, and to the vertical spacing procedures during implantation of the seeds.

The Mick applicator is basically a very simple instrument and its construction is rugged enough so that damage during normal use is practically impossible. Naturally, good care must be taken after each use. All parts should be cleaned and stored in their designated locations. The needles should be placed in the needle holder, which contains four slots for eight needles each. The magazine holder is provided with five holes to store five magazines. The instrument can be cleaned by soaking in hydrogen peroxide immediately after use followed by gentle scrubbing with a soft brush and spraying with jets of water. The sterilization tray can be cleaned with a regular stainless steel cleaning spray. After all parts are correctly stored, it is immediately visible if the set is complete.

PREPARATION FOR USE

The stainless steel tray containing the applicator and accessories should be examined for completeness. All parts should be visually examined and any moving parts should be quickly tested for smoothness of motion. The guide needles should be straight, not crimped, and the points should be sharp.

The first step in preparing the instrument for implantation of I-125 seeds is loading of the magazines. The magazines are stored in the magazine holder of the stainless steel tray and may be removed by unscrewing counter-clockwise (clockwise for storage). The magazine consists of two components: magazine head and cartridge. The magazine head is a hexagonal body containing a plunger under spring tension. The cartridge has a rectangular shape and contains a slot to hold the I-125 seeds. The front of the cartridge is open for loading. The cartridge is best loaded using our V-block (see our leaflet for loading accessories). Pick up the seeds with our special forceps and feed it into the slot from top to bottom. It is important that the seed is not dropped into the cavity, but placed carefully at the bottom of the cartridge. The next seed is picked up in the same manner and fed into the slot until it rests parallel on top of the previous one. This procedure is repeated until the cartridge is filled to capacity of ten (10) seeds. The seeds should slide smoothly and fit across the opening in the front of the cartridge. Seeds which are under or oversized should not be used since they could cause jamming of the magazine or applicator. When the cartridge is loaded to capacity, insert the magazine head plunger into the cartridge slot and turn clockwise with slight downward pressure until it stops. The magazine is now ready for implantation and can be put back into the stainless steel tray.

The entire stainless steel tray and its contents may be sterilized by autoclaving just prior to use. The wooden case is used for transportation and shelf storage only.

Magazines for Au-198 grains are available and work with the same principle, except that the receiving slot is smaller to accommodate the size of the grains. Au-198 magazines are easily identified because of their golden color.

AFTERLOADING TECHNIQUE

The implantation of the I-125 seeds is done by means of an after-loading technique. This technique consists of five basic steps: 1) plan distribution of seeds; 2) insert guide needles; 3) attach applicator to needles; 4 insert magazine containing radioactive seeds and, 5) implant seeds through guide needles.

Using the tumor volume and shape, seed strength, and desired therapeutic dose, the spacing between guide needles and between seeds should be planned so as to achieve the desired therapeutic effect with a minimum of complications. The dosimetry of I-125 seed implants is discussed in *Handbook of Interstitial Brachytherapy*, edited by Basil S. Hilaris, M.D. of Memorial Sloan Kettering Cancer Center (published by Publishing Sciences Group, Inc., Acton, Mass. 1975).

Insertion of guide needles may be accomplished as follows: Insert hollow 17 gauge stainless steel needles, 15 cm long, and ground to a 45 degree point, around the periphery of the tumor mass. (For implants through the intact skin, needles with sharp points are preferrable, but for intrathoracic and intro-abdominal implants, it is better to use less sharp needles that do not penetrate and change their position so easily). For a spherical shaped tumor, 0.55 millicurie nominal seed strength, and an aim of 16000 rads delivered through total decay, needles are usually spaced 1 cm apart for tumors up to 4 cm in diameter, 1.5 cm apart for tumors from 4 cm to 8 cm, and 2 cm apart for larger tumors. All needles should be inserted parallel to each other. The direction of the needles must be considered carefully before starting, so that their position may be palpated and the maximum number of seeds inserted through one needle. Each guide needle is 15 cm long which means that the length of guide needle implanted within a tumor bed may be calculated once the length of protruding needle is known. This will give a guide as to the number of seeds to be inserted in each needle, once the vertical spacing is also determined.

Attachment of the applicator to the guide needles may be accomplished as follows: After all needles have been inserted into the tumor to the required depth, remove applicator instrument from the stainless steel tray. With one hand, hold the instrument in vertical position by inserting thumb and index finger through the finger ring and with the other hand pull out stylet to its extreme end. In order to avoid deeper penetration of the guide needle, a hemostat may be clamped to the needle at the tissue surface prior to attaching the applicator to the needle. Next, lower the applicator instrument over the protruding part of the needle and when it has reached a definite stop, turn the needle chuck-cap clockwise as far as possible.

With the needle firmly attached to the instrument, a pin located in the needle chuck-cap will appear in the middle of the tissue ring cut-out. Check if needle is firmly attached to the instrument by slightly lifting the instrument upward while grasping the needle firmly. Care must be taken at this point not to displace the correctly inserted needle by pulling it out of the tissue.

With one hand hold the main barrel end-cap and with the other hand push down the finger rings. This will bring the tissue ring down to the tissue surface encircling the nose of the hemostat. The hemostat may be removed at this point. The number appearing on top of the black cone on the main barrel indicates the depth of the needle where the first seed should be placed.

Insertion of the seed magazine is as follows. The loaded magazine is taken out of the storage position and inserted all the way into the magazine cubicle of the instrument. Note, that the stylet must be fully retracted out of position in order to allow the cartridge to be inserted. The magazine is firmly in place once a click is heard indicating that the small ball is caught in the indentation of the cubicle and the cartridge slot is facing in the same direction as the slot in the cubicle.

Implantation of the seeds is accomplished as follows. The first of the ten seeds in the cartridge is deposited into the needle by pushing the stylet all the way down. In order to penetrate hard tissue it may be necessary to apply extra pressure to push the wire rod handle as it reaches its end. If the stylet is not completely depressed, the seed will remain in the needle. Palpation of the under side of the tumor mass during this process can generally give assurance that the seed has in fact been deposited at the bottom of the needle.

To insert the next seed, first hold the main barrel of the applicator like a pencil, simultaneously resting the middle and ring fingers against the black cone, and raise the main barrel by two notches if a 1 cm spacing is desired (three notches for 1.5 cm). Pull the stylet out to its extreme end and observe the retraction of the extended plunger in the hexagonal magazine head. This movement indicates that the next seed has placed itself into the proper position in the cartridge for transfer into the guide needle. Repeat procedure. If the plunger does not move, a slight tapping or amount of pressure with the finger tip to the plunger will most likely place the seed into the proper position. If the stylet still does not go through, exchange the magazine and check for deformed seeds. Never force the stylet. After the plunger has dropped completely, the magazine is empty and the stylet can no longer be advanced. A new cartridge may be exchanged in readiness for subsequent seed implantation.

During the implant procedure, it is recommended that the instrument be rinsed frequently in normal saline or heparin solution in order to remove tissue or blood which will interfere with smooth movement of the moving parts of the applicator. A small syringe or asepto is helpful in forcing the solution through the chuck and magazine cubicle areas.

In addition to radiation exposure precautions, an accurate accountability of all sources must be maintained. For this reason, records of sources implanted and remaining sources must coincide with the number of seeds available. All instruments and surgical accessories including sponges and suction devices should be surveyed immediately after the implant procedure. Follow-up of patients may be necessary in order to retrieve sources which are sloughed off post-operatively.

Another danger in use of the applicator for I-125 seeds is the rupture of the outer metal encapsulation. This could occur through excessive use of force in the event of a sticking seed or seed in a cartridge. The tiny ceramic beads containing radioactive I-125 are barely visible once the capsule is ruptured. This can be avoided by proper use of the instrument and sizing of the seeds before use.

An individual familiar with radiation safety procedures and pertinent regulations should be consulted prior to undertaking an implant program in order to assure proper radiation safety of personnel, patient, patient's family, and the general public. A number of guidelines are available through the National Council on Radiation Protection and Measurements, 4201 Connecticut Avenue, NW, Washington, D.C. 20008 and the source suppliers.

CLEANING

Immediately after the implant procedure and before start of the cleaning operations, all guide needles should be checked for possible remaining seeds. This can be accomplished by inserting the loop wire through each needle and observing for any seeds which are ejected from the bottom.

For best results remove tissue and blood from instrument immediately after use. Soaking in hydrogen peroxide or heparin solution should loosen all biological materials. The applicator and accessories should be gently scrubbed with a soft brush and loose materials washed away with a jet of water. A loop wire is included for removing stubborn debris from guide needles. Keeping the instruments clean and in good operating condition insures a precise and efficient implant procedure.

RADIATION SAFETY

Using the Mick applicator and accessories entails handling solid radioactive sources, namely I-125 seeds, Au-198 grains and similar sources. As with any other sources, the principles of time, distance, and shielding should be utilized. Personnel monitoring devices, such as low energy pocket chambers, film badges and thermoluminescence dosimeter devices, should be utilized. Portable shielding devices for bodies and eyes are available as accessories through this company. Lead-rubber gloves are available for surgical manipulation and handling during the implant procedure. These are especially effective for I-125 seed implants because of the low energy of the radionuclide.

[Reprinted from RADIOLOGY, Vol. 105, No. 2, Pages 454-455, November, 1972.]

Rapid Injector for Permanent Radioactive Implantation[1]

Walter P. Scott, M.D.

ABSTRACT: The author presents a simple technique designed to overcome the difficulties inherent in standard implantation methods. This technique may be used with any radioactive seeds now in use.

INDEX TERMS: Therapeutic Radiology, apparatus and equipment • Therapeutic Radiology, interstitial • Therapeutic Radiology, technique

Radiology 105:454–455, November 1972

The implantation of permanent radioactive sources has always suffered from the difficulties of insertion, positioning, and radiation exposure of hospital personnel due to the excessive time required. I wish to describe a simple technique to eliminate these disadvantages which works with any radioactive seeds now in use. Previous experience with this absorbable spacer technique in gynecologic and lung tumors has been free of difficulties or complications; this was particularly true of implantation into a moving target such as the lung. The rapid injection method described here is the final refinement resulting from these early studies.

TECHNIQUE

The seeds are introduced in a column, separated from one another by spacers made of an absorbable material such as #3 surgical gut, rather than being introduced into the tumor individually with a needle or gun. The interval between spacers may very according to the activity of the seed, with a separation of 1.0 cm for seeds ≥ 0.5 mCi and 0.5 cm for seeds <0.5 mCi. The seeds and spacers are lined up alternately within a #17 gauge nylon tube, forming a gas-sterilized cartridge with #19 gauge hypodermic needles inserted in each end to retain the seeds and spacers while allowing the gas to enter. The needles may be removed prior to implantation and replaced with small plugs of sterile bone wax. Using a stylet, the column is transferred into the bore of a #17 gauge needle implanted within the tumor.

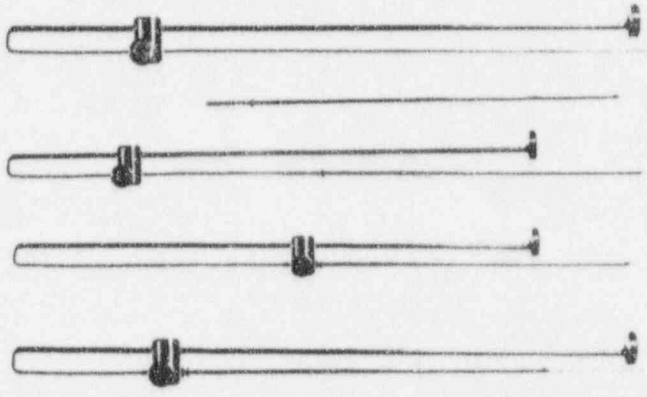


Fig. 1. Photographs of the rapid injector and needle. The bottom three photographs correspond to the positions shown in Figure 2, C, D, and E, respectively.

The stylet is then introduced into the needle until it encounters the column at the distal end of the needle, at which point it is stabilized with one hand while the needle is retracted over it with the other, thus depositing a trail of seeds and spacers in the tumor while those remaining in the needle are later reloaded into new cartridges. Thus all unused (and expensive) seeds are reloaded, and none are wasted. As the seeds decrease in activity, they are loaded in columns with shorter intervals between spacers; again, none are wasted. Variations in dosimetry are possible by adjusting the spacers or using seeds of different activities, *i.e.*, dumbbell loading. Inactive gaps may be left in the tract of the implanted needle by increasing the distance between spacers.

There are several methods of loading the needle. If the tumor is easily accessible, the needle may be preloaded using radium needle forceps prior to implantation, thus facilitating speed, distance, and proficiency. I generally use a standard load consisting of a 5 cm column of 4 seeds, which seems to accommodate tumors of average dimensions. If the needle is inserted more than 5 cm into the tumor, more seeds are added from a new cartridge by first expelling the unwanted seeds; if less than 5 cm, fewer seeds are initially loaded in the same manner. With a surplus of seeds, one could have several cartridges of different loads or load the required number of seeds into the needle from a cartridge of infinite length.

Rapid Injection Technique: Once the needle has been implanted and loaded, the method of injection is the same for all types of sources. Since the last spacer in the column is just below the surface or the tumor, one arm (stylet) of a C-shaped instrument (rapid injector) can be used to advance

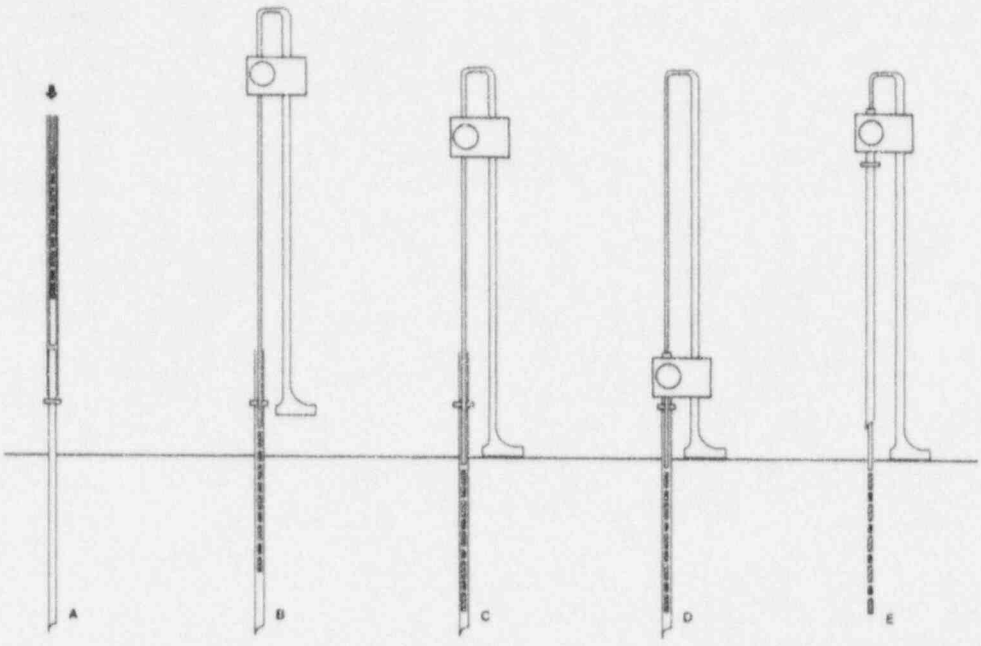


Fig. 2. A. Empty needle within the tumor, ready to receive the column of seeds and spacers from the nylon tube (cartridge).
B. Column of seeds and spacers being transferred to the distal end of the needle by the stylet arm of the rapid injector. The stabilizer arm checks the advance of the stylet and gives it stability as the needle is retracted with the aid of a sliding sleeve-bolt.
C. The column of seeds and spacers has been transferred to the distal end of the needle, using the rapid injector.
D. The sleeve-bolt has been slipped forward to engage the needle prior to retraction.
E. The empty needle has been retracted, leaving a column of seeds and absorbable spacers behind in the tumor.

the seeds to the distal end of the needle while the other arm (stabilizer) checks this advance as its blunt end reaches the surface of the tumor. At this point the needle is retracted with the aid of a sliding sleeve-bolt, leaving the column of seeds and spacers behind in the tumor. This technique is demonstrated in Figure 2, while the rapid injector is shown in Figure 1.

It is possible to expedite the procedure further by eliminating the tube technique and loading the needle directly, implanting it with the aid of radium needle forceps, and injecting the column of seeds and spacers. If they cannot be loaded using a sterile technique, they can still be gas-sterilized.

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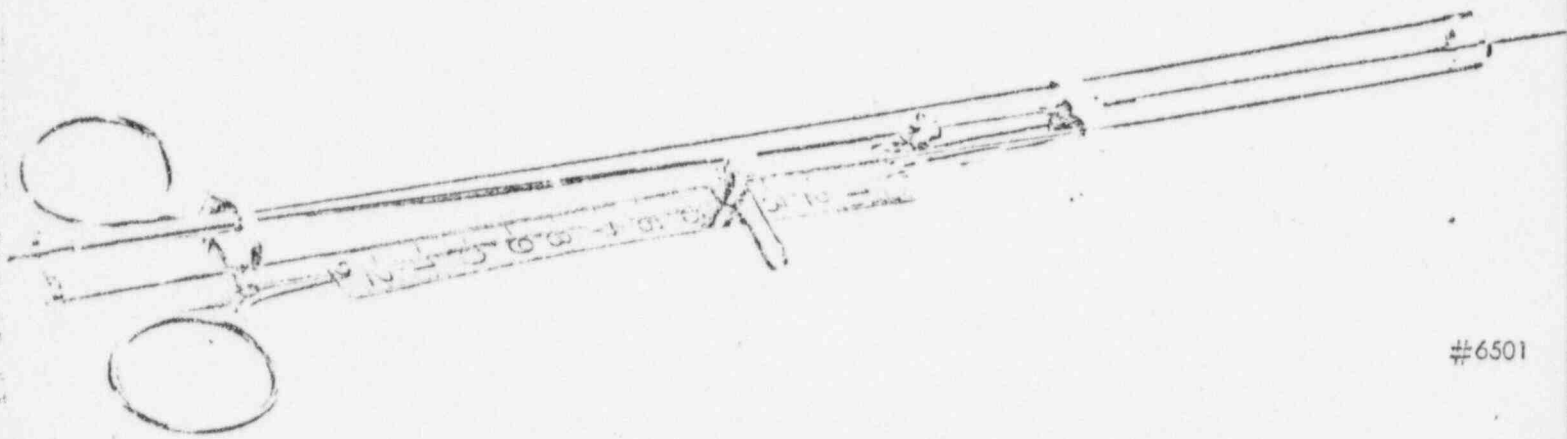
[3] From the Departmen of Radiotherapy and Nuclear Medicine (W. P. S., Director), Cha lotte Memorial Hospital, Charlotte, N. C. 28201. Accepted for publication in July 1972.
The instrument described here is available through Lawrence Soft-Ray Corp., San Jose, Calif.

PERMANET INTERSTITIAL IMPLANT INSTRUMENT

Single seed inserters were replaced in 1956 by U. Henschke, when he developed a new instrument using two distinct afterloading steps, namely, insertion of unloaded hollow needles and afterloading with radioactive sources. The Permanent Interstitial Implant Instrument is commonly used and is the simplest one within the scope of implant instruments.



#6501

First needles are inserted equally spaced by 1 cm within the tumor mass. By measuring the length of the needles outside the tumor, the shape and size of the implanted volume can be determined. The number of sources required to give the desired dose is then calculated. Secondly, the instrument, with its depth gauge is attached to each needle and in turn, through it, the required number of radioactive sources are introduced one by one into the tissue and implanted at the desired depth.

The instrument is provided with a ratched mechanism assuring accurate placement of seeds at any desired depth up to 12 cm. Only one seed can be transferred at a time from pre-loaded stylets. Needles can be withdrawn at 5 mm steps and seeds are manually transferred by means of a stylet into the tumor.

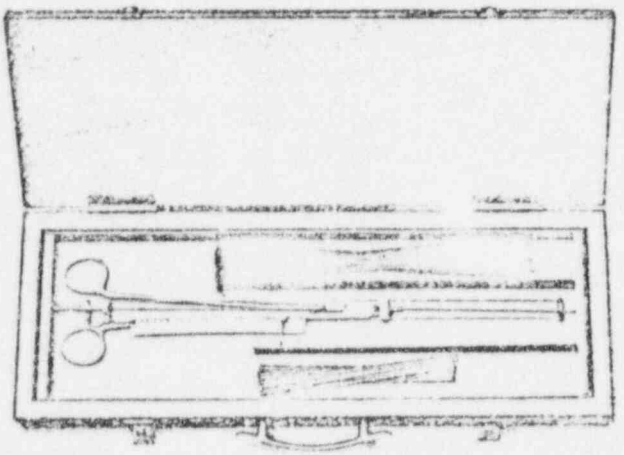
FEATURES:

- lightweight
- easy handling due to simplicity of instrument
- quick exchange of needles due to inherent needle clamping mechanism
- ideal for implants of the prostate but suitable for all implants
- accurate placement of seeds up to 12 cm
- all material stainless steel
- easy cleaning

SET INCLUDES:

1 instrument
32 17 gauge hypodermic needles,
45° point, 15 cm long
75 stylets in Nylon tubing
4 obturators
1 L-ruler
1 15 cm stainless steel ruler
1 stainless steel lift-out tray
1 wooden carrying case

Permanent Interstitial Implant Set



Permanent implants have in the past found their principal indication in palliative cancer treatment. However, with the improved implantation techniques and new radioisotope sources, they are being used more and more for curative therapy as well.

As the first step, unloaded, hollow 17-gauge needles, each 15 cm long, are inserted in and around the tumor. If feasible, the tumor should be so exposed that one hand can be placed under it. By measuring the length of the needles outside the tumor, the shape and size of the implanted volume can be determined. The number of sources required to give the desired dose is then calculated.

As the second step, an instrument with a depth gauge is attached to each needle in turn. Through it the required number of radioisotope sources are introduced one by one into the tissue and implanted at the desired depth.

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- State University of New York at Buffalo

SCHOOL OF MEDICINE
DEPARTMENT OF NUCLEAR MEDICINE
HEALTH PHYSICS

1003

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May 14, 1980

Michael Lamastra
Materials Licensing Branch
United States Nuclear Regulatory
Commission
Washington, D.C. 20555

Dear Mr. Lamastra:

Enclosed is the unofficial report of I-125 seed misadministration requested per our telephone conversation on May 7, 1980. A copy was sent to the Buffalo District FDA Office.

If you need additional information, please call me at (716) 838-5250.

Sincerely,

Bill Quain

Bill Quain, MPH
Health Physicist

ENCLOSURES

BQ/sh

cc: John D. White
Buffalo District
FDA Office

8006170444 4pp

VETERANS ADMINISTRATION MEDICAL CENTER, BLDG. NO. 5
3495 BAILEY AVENUE, BUFFALO, NEW YORK 14215 TEL. (716) 838-5250

Report of Misadministration - Iodine 125 Seeds

Licensee:

Veterans Administration Medical Center
3495 Bailey Avenue
Buffalo, New York 14215
NRC License No. 31-00786-02

Brief description of the event:

A 60 year old male patient was treated May 1, 1980 for cancer of the prostate by interstitial implantation with Iodine-125 seeds. A total of 33 seeds, each 0.5 millicuries, were implanted. The seeds were purchased one week prior to surgery from the Medical Products Division, 3M Company, and were received with a leak test certification.

On May 1, 1980 the seeds were loaded into plastic tube applicators and autoclaved. During the surgery and implantation procedure, difficulty was experienced in transferring the seeds from the applicators to the prostate implant site. Forceps were used to get some of the stuck seed out of the applicators. The stress apparently ruptured the titanium capsule of one or more seeds.

Leakage of the seed(s) was discovered the day after surgery when the patient's urine was assayed for radioactivity (see attached urine data). The patient's thyroid was subsequently blocked with Lugol's and thyroid bioassays conducted. The uptake of I-125 in the thyroid on May 12, 1980 was assayed to be 21.9 microcuries. By May 12, 1980 approximately 280 microcuries of Iodine-125 was excreted in the urine. Based on 10 per cent uptake, the MIRD absorbed dose estimate for the thyroid is 280 rads/mCi (see attached MIRD Report No. 5). The dose to the patients' thyroid is estimated to be 84 rads (300 μCi x 0.28 rad/μCi).

Effect on the patient:

No immediate effect has been observed.

Action taken to prevent recurrence:

Seeds used for future implantation treatments will be gas sterilized prior to surgery. In addition, a recently developed seed applicator gun has been obtained and tested. The gun should prevent stressful treatment of seeds during implantation.

Informed patient:

The patient was informed that one or more seeds unexpectedly leaked and that his thyroid received a radiation dose from the Iodine 125 uptake.

URINE RECORD - I-125 SEED IMPLANT

PATIENTS NAME: _____ # _____

Room Number: _____ DATE OF IMPLANT: May 1, 1980 1069

No. of Seeds Implanted: 33 Total Activity Implanted: 16.5 mCi

Counting Instrument Urine Samples: Beckman 400 gamma counter, serial #8040228

DATE COLLECTED	TOTAL VOLUME	SAMPLE VOLUME	NET cpm URINE SAMPLE	* STD. cpm ~90% Eff.	µCi excreted
5-2-80	0.5 L	1 ml	134,928	118,922	31.5
5-3-80	3.0 L	1 ml	36,622	118,922	55.5
5-4-80	3.0 L	1 ml	22,918	118,922	34.7
5-4-80	1.5 L	1 ml	21,088	118,922	16.0
5-5-80	3.0 L	1 ml	17,102	118,922	25.9
5-6-80	2.4 L	1 ml	18,968	119,999	22.9
5-7-80	2.8 L	1 ml	16,523	119,999	23.4
5-8 80	3.0 L	1 ml	16,524	119,999	25.0
5-9-80	2.7 L	1 ml	14,694	119,999	20.0
5-10-80	3.0 L	1 ml	14,459	119,780	21.9
5-11-80	0.1 L	1 ml	9,893	119,780	0.5
5-12-80	1.0 L	1 ml	7,847	119,390	3.9
					281.2 TOTAL µCi

* I-129 standard, Serial Number H-10, Assayed August 30, 1976.

mird / DOSE ESTIMATE REPORT NO. 5

1063

SUMMARY OF CURRENT RADIATION DOSE ESTIMATES TO HUMANS FROM ^{123}I, ^{124}I, ^{125}I, ^{126}I, ^{130}I, ^{131}I, and ^{132}I AS SODIUM IODIDE

September 1975

SUMMARY OF ESTIMATED ABSORBED DOSES FROM RADIOIODINE AFTER A SINGLE ORAL ADMINISTRATION OF SODIUM IODIDE TO A EUTHYROID ADULT

Target organ	Maximum thyroid uptake (%)	Absorbed dose (rads/mCi of radioiodine administered)						
		^{123}I	^{124}I	^{125}I	^{126}I	^{130}I	^{131}I	^{132}I
Liver	5	0.029	0.36	0.087	0.25	0.32	0.20	0.14
	15	0.028	0.45	0.22	0.45	0.30	0.35	0.13
	25	0.027	0.55	0.36	0.65	0.29	0.48	0.13
Ovaries	5	0.036	0.33	0.029	0.14	0.34	0.14	0.14
	15	0.034	0.31	0.033	0.15	0.31	0.14	0.14
	25	0.031	0.30	0.039	0.15	0.29	0.14	0.13
Red marrow	5	0.030	0.27	0.044	0.16	0.23	0.14	0.094
	15	0.030	0.36	0.077	0.26	0.23	0.20	0.092
	25	0.030	0.46	0.12	0.37	0.23	0.26	0.091
Stomach wall	5	0.25	2.4	0.27	1.5	2.4	1.7	1.2
	15	0.23	2.2	0.26	1.4	2.2	1.6	1.2
	25	0.21	2.0	0.26	1.3	2.0	1.4	1.1
Testes	5	0.013	0.18	0.015	0.088	0.18	0.084	0.078
	15	0.012	0.18	0.018	0.094	0.17	0.085	0.076
	25	0.012	0.17	0.024	0.10	0.16	0.088	0.074
Thyroid	5	2.4	180.0	140.0	320.0	22.0	260.0	2.3
	15	7.5	530.0	450.0	960.0	68.0	800.0	7.4
	25	13.0	890.0	790.0	1,600.0	120.0	1,300.0	13.0
Total body*	5	0.025	0.36	0.11	0.28	0.25	0.24	0.10
	15	0.027	0.59	0.29	0.61	0.27	0.47	0.10
	25	0.029	0.83	0.49	0.95	0.39	0.71	0.11

* Includes dose from source organs plus dose from radioiodine assumed to be distributed uniformly in the total body.

RADIOPHARMACEUTICAL

Sodium iodide as a radiopharmaceutical is supplied in a basic solution to prevent volatilization of the iodine and contains a reducing agent to minimize the conversion to iodate. Liquid and solid forms are available for oral administration as well as sterile solutions for intravenous use; however, most radioiodide is administered orally. The biologic availability of iodide from some solid dose forms may be less than 100%. All production methods for radioisotopes of iodine yield carrier-free products except for ^{131}I. In the case of ^{131}I, the very small quantity of stable iodine does not affect the biologic distribution. For purposes of these dose calculations, the radionuclidic and radiochemical purity of the pharmaceutical have been assumed to be 100%.

NUCLEAR DATA

Nuclear data for the radioisotopes of iodine considered in this report are given in Table 1.

BIOLOGIC DATA

The human tissue distribution data for radioiodine administered as iodide on which this report is based were obtained from the literature and from studies by Henry N. Wellman and his associates at the Nuclear Medicine Laboratory, University of Cincinnati School of Medicine. These data were evaluated by Mones Berman and his associates at the National Institutes of Health and were used as the input data for Berman's model of iodide kinetics (*2*). The thyroid iodide uptake rate constant was then adjusted