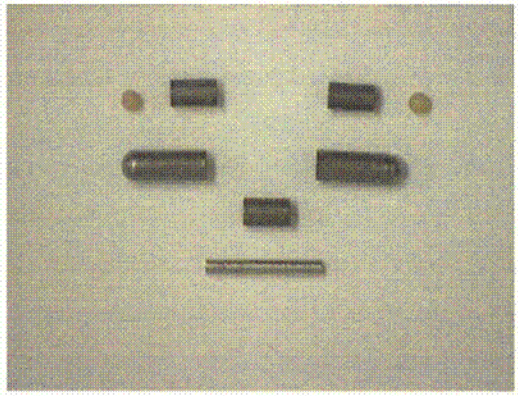
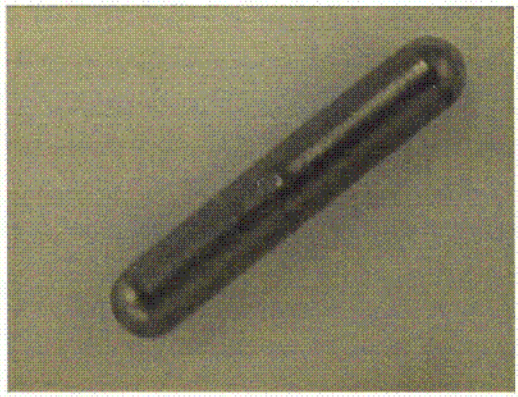
SECTION 3: CONSTRUCTION OF THE PRODUCT – continued

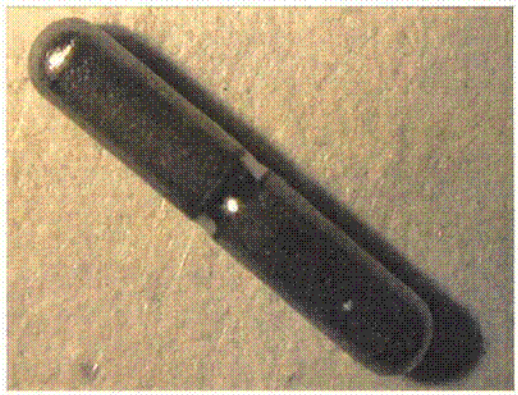
BrachySeed Components



Unwelded BrachySeed



Welded BrachySeed



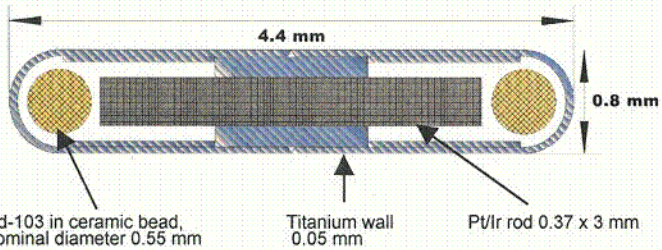
BRACHYSEED™ Pd-103

(DRAXIMAGE Inc. Palladium-103 brachytherapy source, model Pd-1)

DESCRIPTION

Source Design and Construction:
BrachySeed™ Pd-103 is an innovative palladium-103 brachytherapy implant offering a dose distribution in tissue close to isotropic in the therapeutically critical region 0.5 - 2 cm out from the center of the source.

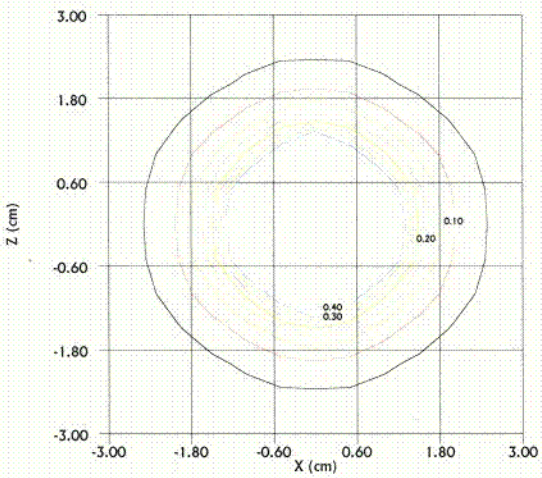
Each BrachySeed™ Pd-103 encapsulates Pd-103 contained in two ceramic beads positioned one at each end. Between the beads lies a platinum/iridium alloy rod whose high density and high atomic number provide for radiographic detection. These components are enclosed in a biocompatible titanium capsule. The capsule is hermetically sealed around the central seam by a laser weld. The design allows little room for movement of the internal parts with consequent predictability of radiation output pattern. The integrity of the structure has been tested according to the standards ISO 2919:1999(E) and ANSI/HPS N43.6-1997.



Radiation Emissions:
Pd-103 decays by electron capture with the emission of characteristic photons. The very low energy electrons emitted are absorbed within the source. The principal photon emissions are 20 and 23 keV gamma-rays. The radiation intensity along the axis of BrachySeed™ Pd-103 at 1 cm from the center is over 90% of that along a transverse-axis at 1 cm. This fluence ratio promotes isotropic dose distribution.

Radiation Dose Distribution:
Current TG-43 data to be used for treatment planning are provided in a document entitled "BrachySeed™ Pd-103 TG-43 Values", available from DRAXIMAGE, Inc.

Iso-dose contours for BrachySeed™ Pd-103 calculated by a Monte Carlo method are shown below. The contours shown are plots of the raw unsmoothed Monte Carlo results.



Isodose contours of the Draximage Pd 103 source based on Monte Carlo calculations. The contours are drawn from 0.05 to 0.4 cGy/U·h at an increment of 0.05 cGy/U·h . The long axis of the seed is in the Z direction

Palladium-103 Decay Factors:
To correct for decay after the assay date of a source, apply one of the following deca factors (DF) based on the Pd-103 half-life of 16.99 days

DAYS		HOURS		
0	1.0000	0.9899	0.9798	0.9699
1	0.9600	0.9503	0.9407	0.9311
2	0.9217	0.9123	0.9031	0.8939
3	0.8848	0.8758	0.8670	0.8582
4	0.8495	0.8408	0.8323	0.8239
5	0.8155	0.8072	0.7990	0.7909
6	0.7829	0.7750	0.7671	0.7593
7	0.7516	0.7440	0.7364	0.7290
8	0.7216	0.7143	0.7070	0.6998
9	0.6927	0.6857	0.6788	0.6719
10	0.6651	0.6583	0.6516	0.6450
11	0.6385	0.6320	0.6256	0.6192
12	0.6130	0.6067	0.6006	0.5945
13	0.5885	0.5825	0.5766	0.5707
14	0.5649	0.5592	0.5535	0.5479
15	0.5424	0.5369	0.5314	0.5260
16	0.5207	0.5154	0.5102	0.5050
17	0.4999	0.4948	0.4898	0.4848
18	0.4799	0.4750	0.4702	0.4654
19	0.4607	0.4560	0.4514	0.4468
	0	6	12	18

ACTIONS
The clinical efficacy of BrachySeed™ Pd-103 implants depends only upon th interaction of the emitted ionizing radiation with the tissue being treated.

INDICATIONS
BrachySeed™ Pd-103 implants with air kerma strengths up to 3.81 U (approx. 3 mC are indicated for permanent interstitial implantation in the treatment of selecte localized tumors such as tumors of the head, neck, lung, pancreas, breast, uterus ad prostate. They can be used either as primary treatment or for residual disease aft excision of the primary tumor or for recurring tumors. They may also be used completion of external beam radiation. BrachySeed™ Pd-103 implants are intende for single use only.
BrachySeed™ Pd-103 implants with strengths greater than 3.81 U (approx. 3 mCi) ar indicated for temporary implantation or surface application to treat localized tumor

CONTRAINDICATIONS
The application of BrachySeed™ Pd-103 to tumors in generally poor condition (e. ulcerated) which would allow substantial source migration is not recommended.

ADVERSE REACTIONS
Exposure to Radiation:
Since BrachySeed™ Pd-103 achieves its therapeutic effect through the delivery radiation to target tissue, any adverse event associated with tissue radiation dama may theoretically be associated with its use. With implantation of low energy source in the prostate, impotence may arise in about 25% of cases and urinary incontinen and prostatitis have been reported in about 1% of cases. After prostate implant transient dysuria and increased urinary frequency have been reported in about 15 of patients.

Biocompatibility:
BrachySeed™ Pd-103 implants are hermetically sealed titanium capsules. Experience has shown that when titanium is used to completely encapsulate radioactive source for implant, the danger of adverse tissue reaction is not significa and there have been no adverse reactions reported.

WARNINGS AND PRECAUTIONS
Source Manipulations:
A damaged source may release Pd-103 into the environment or, if medically applie into body fluids. If a source has been visibly damaged, seal it in a container a discard it immediately to radioactive waste and check the area for contamination
Under no circumstances should damaged sources be implanted.
Do not force BrachySeed™ Pd-103 implants into (or from) any piece of equipmen Doing so may damage a source. With respect to sources used for temporary implan and reuse, when loading or removing sources from after-loading catheters, it advisable to use a vented chemicahood which has adequate air flow. If a sharp too is used to remove sources from after-loading catheters, use extra care.
To assure that sources have not been damaged following removal from equipmen a contamination survey should be conducted using a radiation monitor capable detecting 20 keV photons. This survey should include wipe (or leak) tests of source and an overall area survey.

Source Vibration, Shock and Elevated Temperatures:
Do not expose BrachySeed™ Pd-103 implants to undue vibration or shock, temperatures above 150°C for any period or temperatures above 100°C for more than 2 hours.

Source Corrosion:
The BrachySeed™Pd-103 capsule has excellent corrosion resistance. However, do not expose a source to acid or alkaline solutions exceeding one molar. The sources are not affected by common solvents such as acetone and alcohol or by mild detergents.

Personnel Monitoring:
BrachySeed™ Pd-103 implants are radioactive and appropriate precautions must be taken when handling them. All steps of the implantation procedure should be planned in advance to minimize radiation exposure to personnel.Personnel monitoring is required. Typically a film or TLD dosimeter worn on the body and a ring dosimeter (during source handling) is adequate.

Shipping Container:
BrachySeed™ Pd-103 implants are shipped in a screw-capped vial or pre-loaded magazine inside a lead container which shields >99.9% of the radiation from Pd-103. The lead container may be used for storage and transport of seeds within the hospital.

Source Handling and Storage:
BrachySeed™ Pd-103 implants should be handled behind shielding of adequate thickness. A sheet of lead of thickness 0.25 mm will reduce the exposure by >99%. Forceps should be used to maintain operator to source distance. Only gentle pressure should be applied so that sources are not damaged.BrachySeed™Pd-103 implants should not be picked up with the fingers. When in doubt about the fit of BrachySeed™Pd-103 implants into various source containers, tubes, magazines and applicators, load the containers first with non-radioactive sources to determine their compatibility with the sources. Packages of non-radioactive BrachySeed™ Pd-103 implants are available from DRAXIMAGE Inc. (see contact details at end of this sheet).
BrachySeed™Pd-103 implants should be stored in the shipping vial and lead pot in a secure area and according to the user's Federal , State or Provincial licence.

Accidental Source Damage:
Although BrachySeed™ Pd-103 implants have a high structural integrity, it is possible through rough handling to rupture a source causing it to release Pd-103. If this happens, the area of the accident should be closed off; the sources should be sealed in a container; personnel movement should be controlled to avoid spread of any radioactive contamination; and the area and personnel should be decontaminated according to established procedures.

Source Sterilization:
BrachySeed™ Pd-103 implants with the marking "non-sterile" on the package label must be sterilized in an adequately shielded container before implantation, using steam or ethylene oxide (EtO). Do not use dry heat or chemical sterilization.
Steam Sterilization (autoclave): Use the normal cycle (121°C at 15 psi for 15 to 30 minutes) or the flash cycle (133°C at 30psi for 3 minutes). Autoclaves should be equipped with traps or other means to prevent seed loss through the drain hole.
Ethylene Oxide (EtO) Sterilization: Use cycle and aeration times recommended by the manufacturer of the sterilizer or use those determined at the hospital.
BrachySeed™ Pd-103 implants may be loaded into various sorts of cartridges designed to be used with applicators.Use care when sterilizing sources loaded into plastic tubes as steam heat may warp the tubes and prevent source recovery.

Application to Patient:
BrachySeed™Pd-103 implants 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 government agency. Radiation detection equipment capable of detecting 20keV photons should be available whenever the sources are being handled.
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, 3].

Treatment of Patient:
All patients should be informed of the nature of BrachySeed™ Pd-103 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 a BrachySeed™ Pd-103 implant. Guidelines for necessary precautions have been established [4].
All patients should be advised of the possibility that one or more BrachySeed™ Pd-103 implants might become detached as a tumor regresses. Under these circumstances, any bandages or linens which come into contact with the site of the implant should be scrutinized for small metallic tubes about 0.6 cm (1/4 inch) long and 0.8 mm (1/32) inch thick. Patients should be advised that whenever sources 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 institution where the implant procedure was done should be notified of such an event as soon as possible after its occurrence.

Accountability/Disposal:
Palladium-103 is an accountable radioactive material. BrachySeed™ Pd-103 implants must be strictly controlled and stored in a locked safe. If any significant amount material cannot be accounted for, the loss must be reported to the appropria licensing agency. When disposal is indicated, BrachySeed™ Pd-103 implants shoul be transferred to an authorized radioactive waste disposal agency, and not dispose of in normal waste.

Leak Testing:
Each BrachySeed™Pd-103 implant has been leak-tested prior to shipment and ha shown <0.005 microcuries of removable Pd-103. This value is printed on th Certification Form that accompanies each shipment. Each BrachySeed™ Pd-10 must be leak-tested at intervals not exceeding six months until disposed of.

DOSAGE AND ADMINISTRATION
Established practice [5, 6, 7, 8, 9] should be followed for the calculation of the total activi to be implanted, the proper placement of the sources within the tissue, and th evaluation of the radiation dose distribution achieved. Dose distribution around ea individual source is close to, but not perfectly, isotropic and the degree of anisotrop should be allowed for in patient dose calculations. TG-43 data are provided in th document entitled "BrachySeed™ Pd-103 TG-43 Values", available from DRAXIMAGE, Inc. Confirmation of seed activity can be achieved using a well-typ ionization chamber calibrated for BrachySeed™ Pd-103 by an accredited ADCL.

DIRECTIONS FOR USE
BrachySeed™ Pd-103 implants with the marking "non-sterile" on the packag label must be sterilized before use. (See above for sterilization guidance). Durin the treatment procedure, the patient must be appropriately anaesthetized. A qualifie practitioner is to place the BrachySeed™Pd-103 implants on or throughout the tumo volume according to a treatment plan. Commercially available applicators an needles may be used.

HOW SUPPLIED
BrachySeed™Pd-103 air-kerma strengths are traceable to the corrected 1999 NIS standard. They are available in strengths from 0.1 to 50U (microGray meter square per hour, uGy-m²/h), i.e. apparent activities approximately 0.08 to 40millicuries. Th sources are packaged in a screw-capped vial secured in a lead container. Th container label provides information on air-kerma strength, apparent activity per seed total activity, assay date, number of sources, and an order identity number. The va is similarly labeled. Any discrepancies in labeling or against the order paperwo noted upon receipt of the product must be reported immediately to DRAXIMAGE In (see contact details at end of this sheet). BrachySeed™ Pd-103 implants a supplied either non-sterile or sterilized and either loose or in pre-loaded magazine

LICENSING
The Canadian Nuclear Safety Commission has approved BrachySeed™ Pd-10 implants for distribution to persons properly licensed for its use in Canada. Provinci law restricts this device to sale by or on the order of a physician. The US-Nucle Regulatory Commission has approved BrachySeed™ Pd-103 implants for distributio to persons properly licensed for its use in the United States. US Federal law restric this device to sale by or on the order of a physician.

REFERENCES

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DRAXIMAGE

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Distributed in the U.S. by
Cytogen Corporation
Princeton NJ 08540

Figure 2a. LABELLING FOR NON-STERILE SOURCES

Outer Container Label

CAUTION - RADIOACTIVE MATERIAL
Sealed sources - handle with care and store in this container or similar. See the handling, storage and leak testing instructions in the WARNINGS AND PRECAUTIONS section of the package insert.

BrachySeed™Pd-103, Model Pd-1, Palladium-103 Brachytherapy Source
[Product code] 502200
Total apparent activity: _____ (mCi) Palladium-103
Apparent activity per source: _____ (mCi)
Number of sources: _____
Avg. air-kerma strength _____ U
Assay date: _____
Lot number: _____

The U.S. Nuclear Regulatory Commission has approved distribution of the Pd-1 to the persons licensed to use byproduct material identified in 35.57, 35.400, or 35.500 of 10 CFR, as appropriate, and to persons who hold an equivalent licence issued by an Agreement State.

WARNING: NON-STERILE - SINGLE USE ONLY

DRAXIMAGE Inc., Kirkland QC, Canada H9H 4J4

Distributed in the U.S. by Cytogen Corp. Princeton, NJ 08540

Primary container label:

CAUTION PALLADIUM-103
RADIOACTIVE MATERIAL
BrachySeed™Pd-103, Model Pd-1
Brachytherapy Source
[Product Code] 502200
Lot No. _____
Number of sources _____
Total activity: _____ mCi
Assay date: _____
NON-STERILE
DRAXIMAGE Inc. Canada

Warning insert

CAUTION - RADIOACTIVE MATERIAL

READ **WARNINGS AND PRECAUTIONS** SECTION OF THE PACKAGE INSERT SHEET IN THIS PACKAGE BEFORE HANDLING THIS CONTAINER

Figure 2b: LABELLING FOR STERILE SOURCES

Outer Container Label

CAUTION – RADIOACTIVE MATERIAL
Sealed sources - handle with care and store in this container or similar. See the handling, storage and leak testing instructions in the WARNINGS AND PRECAUTIONS section of the package insert.

BrachySeed™Pd-103, Model Pd-1, Palladium-103 Brachytherapy Source
*[Product code]*503160
Total apparent activity: _____ (mCi) Palladium-103
Apparent activity per source: _____ (mCi)
Number of sources: _____
Avg. air-kerma strength _____ U
Assay date: _____
Lot number: _____

The U.S. Nuclear Regulatory Commission has approved distribution of the Pd-1 to the persons licensed to use byproduct material identified in 35.57, 35.400, or 35.500 of 10 CFR, as appropriate, and to persons who hold an equivalent licence issued by an Agreement State.

WARNING: STERILE - SINGLE USE ONLY

DRAXIMAGE Inc., Kirkland QC, Canada H9H 4J4

Distributed in the U.S. by Cytogen Corp. Princeton, NJ 08540

Primary container label:

CAUTION PALLADIUM-103
RADIOACTIVE MATERIAL
BrachySeed™Pd-103, Model Pd-1
Brachytherapy Source
[Product Code] 503160
Lot No. _____
Number of sources _____
Total activity: _____ mCi
Assay date: _____
STERILE
DRAXIMAGE Inc. Canada

Warning insert

CAUTION - RADIOACTIVE MATERIAL

READ **WARNINGS AND PRECAUTIONS** SECTION OF THE PACKAGE INSERT SHEET IN THIS PACKAGE BEFORE HANDLING THIS CONTAINER