

For Single Use, R_x ONLY, Non-Sterile

Description

Proxcelan™ Cesium-131 Brachytherapy Seeds

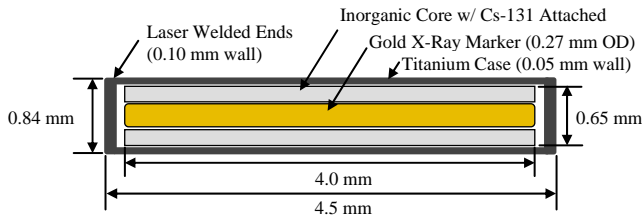
Non-Sterile Implant Device containing Model CS-1, (Rev.2) Seeds:

PL-4 - Cs-131 Preloaded Mick® Cartridges – Non-Sterile

Non-Sterile Cesium-131 Loose Seeds:

Cs- 131 Brachytherapy Seed Model CS-1, (Rev. 2) – Non-Sterile

The functional component of the Proxcelan preloaded Mick cartridges is the Proxcelan brachytherapy seed. The Proxcelan brachytherapy seed consists of a welded titanium capsule containing the low energy gamma (X-ray) emitting isotope, Cesium-131, adsorbed onto an internal inorganic substrate. The seed configuration is designed to generate near isotropic emission of therapeutic radiation.



Physical Characteristics

Principle Radionuclide:	Cesium-131	(Cs-131)
Half-life of Cs-131:	9.69 days	(232.6 hr)
Radiation Energy:	29.5, 29.8, 33.6 keV	
Half-Value Thickness:	0.025 mm of Lead	
Average Dose Rate Constant:	1.059 cGy/U·Hr.	
Decay Mode:	Cs-131 decays by electron capture with the emission of characteristic low-energy X-ray photons and electrons. The electrons are absorbed by the titanium wall of the seed.	
Radionuclide Purity:	> 99.85%	Cs-131
	< 0.1%	Cs-132
	< 0.05%	All other radioisotopes

Indications

Proxcelan preloaded Mick cartridges are indicated for the treatment of malignant disease (e.g., head and neck, eye, brain, breast, prostate, etc.) and may be used in surface, interstitial, and intracavitary applications for tumors with known radiosensitivity. The seeds may be used as a primary treatment or in conjunction with other treatment modalities, such as external beam radiation therapy, chemotherapy or as treatment for residual disease after excision of primary tumors⁽¹⁾. The Proxcelan preloaded Mick cartridges have the same indications for use as Proxcelan brachytherapy seeds, Model CS-1.

Contraindications

As with other brachytherapy sources, treatment of tumors in general poor condition (e.g. ulcerated) is not recommended with Proxcelan preloaded Mick cartridges, due to potential for source migration.

Warnings

Proxcelan Preloaded Mick Cartridges and loose brachytherapy seeds must be sterilized prior to implantation using a qualified sterilization procedure. IsoRay recommends the following sterilization procedures:

Preloaded Mick Cartridges: Steam sterilize Proxcelan preloaded Mick cartridges in the stainless steel pig at 123° C (253°F) for 34 minutes. Prior to sterilization, wrap the stainless steel pig in approved autoclave wrap or seal it in a breather bag appropriate for steam sterilization in order to maintain sterility.

Loose Seeds: Steam sterilize loose seeds at 121° C (250°F) for 30 minutes. For adequate steam penetration, remove the lids from the stainless steel container or the outer lead shielding container and the inner glass vial containing the seeds. Sterilize the seeds in the stainless steel container or glass vial and lead container as well as the separated lids. USING ASEPTIC TECHNIQUE, replace the lids on the stainless steel container or glass vial and the lead container. The stainless steel container or glass vial and lead container should be upright during the sterilization process.

As a precaution, the steam autoclave should be equipped to prevent seed loss through the condensate drain in the event that seeds are spilled inside the autoclave. DO NOT USE COLD CHEMICAL STERILIZATION. Some cold chemical sterilization solutions may leave a residue which can interfere with seed loading and implantation.

Damaged Devices or Seeds: Never implant visibly damaged Proxcelan preloaded Mick cartridges or loose Proxcelan brachytherapy seeds.

Proxcelan preloaded Mick cartridges and loose Proxcelan brachytherapy seeds should not be handled roughly or forced into (or from) any implant tube, needle, or cartridge, since this may breach the external casing, potentially releasing Cs-131 into the environment and/or body fluids if implanted. If this should happen, close off the area, seal the seeds in a shielded container, restrict personnel movement to avoid spread of any radioactive contamination, and survey/decontaminate the area and personnel according to established radiological procedures.

Precautions

Caution: Proxcelan preloaded Mick cartridges and loose Proxcelan brachytherapy seeds contain radioactive Cs-131.

Proxcelan preloaded Mick cartridges and loose Proxcelan brachytherapy seeds should only be handled in authorized, licensed facilities by experienced personnel who are fully trained and qualified in the safe use of radioactive materials by the appropriate regulatory agency. The Proxcelan brachytherapy seeds are quite small and are visually difficult to locate if dropped. All radiation and contamination surveys should be completed using calibrated equipment that is capable of detecting 30 keV photons (low energy X-rays). Personnel monitoring for radiation exposure is required (e.g., film badge, thermal luminescent dosimeter, finger rings, etc.). The cesium-131 half-value thickness of lead is 0.025 mm. Thus, a 0.25 mm lead sheet will provide ~99.9% reduction of exposure.⁽²⁾

Caution: Proxcelan preloaded Mick cartridges and loose Proxcelan brachytherapy seeds exhibit a high surface dose rate.

Appropriate precautions must be taken during handling. (e.g., keep devices shielded, away from personnel, and minimize exposure time). Plan the implantation procedure to minimize radiation exposure to personnel.^(3,4) The devices should be handled behind shielding of adequate thickness. Forceps, either reverse or normal action, should be used to maintain adequate distance. If normal action forceps are used, gentle pressure should be applied so that the devices are not damaged. **IMPLANT DEVICES OR LOOSE SEEDS SHOULD NOT BE PICKED UP WITH THE FINGERS.**

Caution: Do not expose Proxcelan preloaded Mick cartridges or loose Proxcelan brachytherapy seeds to extreme environmental conditions.

Proxcelan brachytherapy seeds have an outer titanium shell which has excellent biocompatibility and stability under normal use. The seeds are not affected by moderate pressure, vacuum, temperature, common solvents (e.g., acetone, alcohol, etc.), or mild detergents. Do not expose the seeds to strong acids or bases. Do not expose seeds to excessive temperatures greater than 300°C or pressures greater than 100 psi.

Caution: Caution is necessary if a post-implant transurethral resection of the prostate (TURP) is required due to the possibility of damaging the implanted seeds and the potential for a seed to be removed resulting in a risk of radiation exposure to staff.

Instructions for Use

Model PL-4 consists of Proxcelan Model CS-1 seeds preloaded into disposable Mick® cartridges and may only be implanted with a Mick® Applicator. **This product has been supplied non-sterile and MUST BE STERILIZED PRIOR TO USE.**

Loose non-sterile Proxcelan brachytherapy seeds may accompany an order for Proxcelan implant devices. **The Proxcelan model CS-1 loose seeds are supplied non-sterile in a stainless steel shielded containers or shielded glass vials and MUST BE STERILIZED PRIOR TO USE.** Loose seeds may be implanted using standard brachytherapy implant techniques, e.g., 18 gauge UTW brachytherapy needle, seed applicator, brachytherapy sleeves, etc.

Radiological protection devices should be utilized during implantation procedures. When protective barriers are not practical, (e.g., certain surgical stages), the user must rely on time and distance to minimize radiation.

Determination of Source Shelf-Life

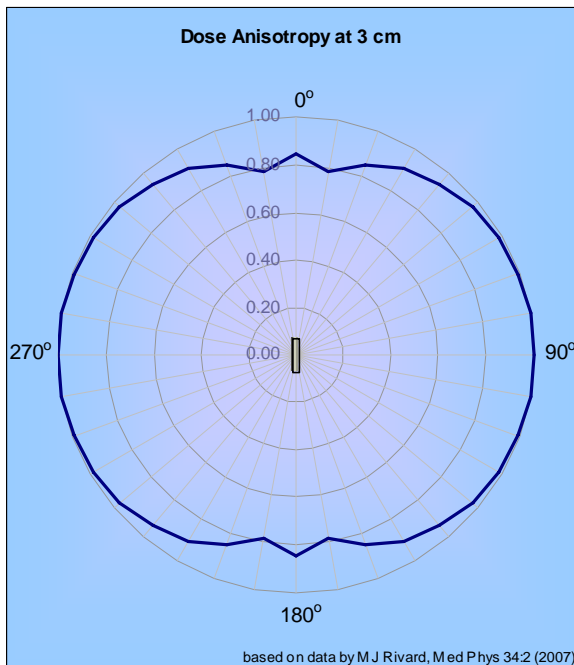
The Proxcelan brachytherapy seeds in preloaded Mick cartridges contain cesium-131 with a 9.69 day half-life and must be corrected for decay in order to properly calculate activity at the time of implantation as shown in the table below:

Day	Factor	Day	Factor	Day	Factor
0	1.0000	11	0.4553	22	0.2073
1	0.9310	12	0.4238	23	0.1930
2	0.8667	13	0.3946	24	0.1796
3	0.8069	14	0.3673	25	0.1672
4	0.7512	15	0.3420	26	0.1557
5	0.6993	16	0.3184	27	0.1449
6	0.6510	17	0.2964	28	0.1349
7	0.6061	18	0.2759	29	0.1256
8	0.5643	19	0.2569	30	0.1170
9	0.5253	20	0.2392	31	0.1089
10	0.4890	21	0.2226	32	0.1014

Dosage and Administration

The total activity and placement of Proxcelan brachytherapy seeds in preloaded Mick cartridges required for any given treatment depends on a number of well-established factors (e.g. treatment goals, tumor location/volume/shape, radiation history of the tumor site, concurrent treatments, etc.). Established practice should be followed for the proper placement of sources within the tissue and for evaluation of the radiation dose distribution achieved during implantation.⁽⁵⁻¹⁰⁾

The Proxcelan brachytherapy seed is designed to produce a nearly isotropic dose distribution. The radiation dose contour of the Proxcelan brachytherapy seed at a radius of 3 cm from the source appears in the figure below.



The dose characteristics of Proxcelan brachytherapy seeds have also been confirmed through extensive Monte Carlo evaluations in accordance with American Association of Physicists in Medicine (AAPM) Task Group 43 guidelines.^(5, 11) Proxcelan preloaded Mick cartridges and loose Proxcelan brachytherapy seeds are available with Air-Kerma strengths from 0.1 to 27 U [microGray meter squared per hour ($\mu\text{Gym}^2/\text{h}$)]⁽¹²⁻¹⁵⁾.

AAPM guidelines for brachytherapy should be followed for independent verification of source output.⁽⁵⁻⁷⁾ A certificate of analysis is provided with each shipment that includes: customer order number, lot number, number of seeds, reference date, implant date, and average and total activities expressed as apparent activity (mCi) and Air Kerma strength ($\mu\text{Gym}^2/\text{h}$) traceable to NIST (National Institute for Standards and Technology). Additional information, including patient and physician names, may be provided upon request.

Adverse Reactions

The potential for, and symptoms of, adverse events related to radiation exposure will vary depending on the radiosensitivity of the exposed tissue, the amount of radiation delivered, and the placement of the seeds themselves. The following information has been derived from articles published in the medical literature.

Mild to moderate genitourinary and gastrointestinal events have been documented in the general literature regarding the tolerability of brachytherapy. Immediately subsequent to transperineal seed implantation for prostate brachytherapy, there is often procedure-related bleeding or burning beneath the scrotum or passage of blood in the urine.⁽¹⁶⁾ These symptoms are usually treated supportively. Short-term urinary symptoms (e.g., frequent urination, discomfort, or difficulty voiding), similar to Iodine-125 brachytherapy have been reported with Proxcelan seeds. These symptoms are generally mild to moderate and often resolve quickly within 4 - 6 months.⁽¹⁷⁻²⁰⁾ Impotence has been noted as a possible long-term adverse effect of brachytherapy which may be age-related and often dependent on pretreatment factors.⁽²¹⁾ Long-term incontinence is uncommon,⁽²⁰⁻²²⁾ although patients who have previously undergone transurethral resection of the prostate (TURP) may be at a higher risk.^(20,23) Urethral stricture after brachytherapy has been reported in a small percentage of cases.^(20, 24) Rectal complications associated with prostate seed implantation, (e.g. fecal incontinence and rectal bleeding), have been reported in the literature.^(17,25) Incidents of asymptomatic seed embolization to the lungs associated with brachytherapy seeds have been reported in the general literature.⁽²⁶⁾

Patient Counseling Information

All patients should be informed of the nature of Proxcelan brachytherapy seeds in preloaded Mick cartridges 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 Proxcelan brachytherapy seeds. Guidelines for necessary precautions and patient release have been established.⁽²⁷⁻²⁹⁾

All patients should be advised of the possibility that, during a course of treatment, one or more seeds may be released into the urine or semen. Bandages or linens which come into contact with the implant site should be scrutinized for small metallic seeds (4.5 mm long). Patients should be advised that whenever seeds are found, they should be picked up with a spoon, placed in a jar or other container, and stored in an uninhabited area in the home. Patients should notify their health care provider as soon as possible after such an occurrence.

Patients should be informed to advise their physician of the implant if a transurethral resection of the prostate (TURP) is considered due to the possibility of damaging the implanted seeds and the potential for a seed to be removed resulting in a risk of radiation exposure to staff.

Accountability

Proxcelan preloaded Mick cartridges may only be distributed to persons licensed pursuant to Washington State Department of Health (WDOH) regulations or under equivalent licenses of the U.S. NRC (Nuclear Regulatory Commission) or an Agreement State, and outside the United States, to persons authorized by the appropriate authority.

As with all radioactive materials, Proxcelan preloaded Mick cartridges must be controlled in accordance with approved procedures by authorized personnel in licensed facilities. When not in use, Proxcelan preloaded Mick cartridges and loose seeds should be stored in shielded containers in a controlled area. (Additional user requirements may also apply.) If any radioactive material cannot be accounted for, the loss must be reported to the appropriate state or federal licensing agency.

Immediately report any discrepancies between ordered and received shipments or any damaged or misrouted shipments to IsoRay Medical, Inc. Customer Service. Dispose of damaged or unused Proxcelan preloaded Mick cartridges or loose seeds in compliance with local, state and federal regulations. If seed disposal services are desired, contact IsoRay Customer Service for return authorization at **1-509-375-5329**. Radioactive materials approved for return must comply with all applicable U.S. Department of Transportation regulations (49 CFR 173) regarding packaging and labeling.



Leak Testing

Each Proxcelan brachytherapy seed is leak tested prior to shipment and has passed a leak test showing < 0.005 μCi of removable Cs-131 as required by Washington State Department of Health (WDOH) regulations. The leak test date and value are printed on a certificate of analysis with each shipment. The user is not required to perform additional leak testing.

Literature Citations And References

1. Hilaris, BS, (ed.) Handbook of Interstitial Brachytherapy. Publishing Sciences Group Inc., Acton, Massachusetts (1975).
2. Henschke, UK, Lawrence, DC, "Cesium-131 Seeds for Permanent Implants," Radiology, 85, 1117-1119 (1965).
3. Protection of Radiation from Brachytherapy Sources. NCRP Report No. 40, Washington DC (1972).
4. Radiation Protection for Medical and Allied Health Personnel. NCRP Report No. 48, Washington DC (1976).
5. Rivard MJ, Coursey BM, DeWerd LA, Hanson WF, Huq MS, Ibbot GS, Mitch MG, Nath R, and JF Williamson, "Update of the AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations", Med. Phys., 31, 633-674 (2004).
6. Nath R, Anderson LL, Meli JA, Olch AJ, Stitt JA, and Williamson JF, "Code of Practice for Brachytherapy Physics: Report of the AAPM Radiation Therapy Committee Task Group No. 56," Med. Phys. 24, 1557-1648 (1997).
7. J. F. Williamson, B. M. Coursey, L. A. DeWerd, W. F. Hanson, and R. Nath, "Dosimetric Prerequisites for Routine Clinical Use of New Low Energy Photon Interstitial Brachytherapy Sources," Med. Phys. 25, 2269-2270 (1998).
8. Dale, RG, "Radiobiological Assessment of Permanent Implants Using Tumour Repopulation Factors in the Linear-Quadratic Model", Br. J. Radiol. 62, 241-243 (1989).
9. Williamson, JF, Coursey, BM, DeWerd, LA, Hanson, WF, Nath, R, Rivard, MJ, and Ibbott, GS, "On the use of Apparent Activity (App) for Treatment Planning of I-125 and Pd-103 Interstitial Brachytherapy Sources: Recommendations of the American Association of Physicist in Medicine Radiation Therapy Committee Subcommittee on Low-Energy Brachytherapy Source Dosimetry," Med. Phys. 26, 2529-2530 (1999).
10. Anderson, LL, "Interstitial Brachytherapy – Physical, Biological, and Clinical Considerations," Interstitial Collaborative Working Group, Raven Press, New York, NY 1990.
11. Rivard MJ. "Brachytherapy dosimetry parameters calculated for a ¹³¹Cs source," Med. Phys. 34(2), pp. 754-762 (2007).
12. Murphy, MK, Piper RK, et al., "Evaluation of the new Cesium-131 seed for use in low energy X-ray brachytherapy," Med. Phys. 31(6), pp.1529-1538 (2004).
13. ICRU Report 60, "Fundamental Quantities and Units for Ionizing Radiation", International Commission on Radiation Units and Measurements, Bethesda, MD (1988).
14. Mitch, MG, Zimmerman, BE, Lamperti, PJ, Seltzer, SM and Coursey, BM, "Well Ionization Chamber Response Relative to NIST Air-Kerma Strength Standards for Prostate Brachytherapy Seeds," Med. Phys. 27, 2293-2296 (2000).
15. "X-Ray and Gamma Standards for Detector Calibration," International Atomic Energy Agency, Tech Doc-619, September, p.149 (1991).
16. Storey MR, Landgren RC, Cottone JL, et al., "Transperineal ¹²⁵Iodine Implantation for Treatment of Clinically Localized Prostate Cancer: 5-year Tumor Control and Morbidity", Int. J. Radiat. Oncol. Biol. Phys. 43(3), 565-570 (1999).
17. Prestige B, and Bice W, "Results of a Multi-Institutional Trial Using Cesium—131 Permanent Prostate Brachytherapy" Int. J. Radiat. Oncol. Biol. Phys. 69(3), S333 (2007).
18. Moran BJ and Braccioforte MH, "Urinary Morbidity Following Cs-131 Brachytherapy for Localized Prostate Cancer," Int. J. Radiat. Oncol. Biol. Phys. 69(3), S378 (2007).
19. Blasko JC, Grimm PD, Ragda H, Schumacher D. "Implant Therapy for Localized Prostate Cancer" in Prostate Cancer, (Ernstoff MS, Heaney JA, Peschel RE, ed.) Blackwell Science, Cambridge, Massachusetts, and Oxford, England. pp.137-155 (1998).
20. Stock RG, Stone NN, DeWyngaart JK, et al., "Prostate Specific Antigen Findings and Biopsy Results Following Interactive Ultrasound Guided Transperineal Brachytherapy for Early Stage Prostate Carcinoma", Cancer 77(11), 2386-2392 (1996).
21. Wallner K, Roy J, Harrison L, "Tumor Control and Morbidity Following Transperineal Iodine-125 Implantation for T1/T2 Prostatic Carcinoma", J. Clin. Oncol. 14, 449-453 (1996).
22. Blasko JC, Grimm PD, Ragde H, "Brachytherapy and Organ Preservation in the Management of Carcinoma of the Prostate", Sem. Radiat. Oncol. 3, 240-249 (1993).
23. Stone NN, Stock RG, "Prostate Brachytherapy: Treatment Strategies", J. Urol. 162, 421-426 (1999).
24. Peschel RE, Chen Z, Roberts K, Nath R., "Long-Term Complications with Prostate Implants; Iodine-125 vs. Palladium-103", Radiat. Oncol. Invest. 7, 278-288 (1999).
25. Waterman FM and Dicker AP, "Probability of Late Rectal Morbidity in ¹²⁵I Prostate Brachytherapy," Int. J. Radiat. Oncol. Biol. Phys., 55(2), 342-353 (2003).
26. Tapan EM, Blasko JC, Grimm PD, et al., "Reduction of Radioactive Seed Embolization to the Lung Following Prostate Brachytherapy", Int. J. Radiat. Oncol. Biol. Phys. 42(5), 1063-1067 (1998).
27. Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides. NCRP Report No. 37, Washington DC (1970).
28. U.S. NRC. Criteria for the Release of Individuals Administered Radioactive Material. Office of the Federal Register. 10CFR Parts 20 and 35:62FR 4120 (1997).
29. U.S NRC, Release of Patients Administered Radioactive Materials, NUREG 1556, Vol. 9, Appendix U.