



BEBIG

An Eckert & Ziegler Company

IsoSeed[®] I-125

(I25.S06)

Instructions for Use

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The instructions for use contain important information on the handling and use of the product and the safety measures which have to be taken. Please read the instructions carefully before any handling or use of the product.

1. MANUFACTURER

BEBIG Isotopen- und Medizintechnik GmbH
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2. DESCRIPTION OF PRODUCT

The IsoSeeds[®] I-125 are brachytherapy sources which are implanted in tissue for the treatment of localised tumours, especially in the prostate. The seeds remain in the body after the conclusion of the therapeutic effect, i.e. after radioactive decay is completed.

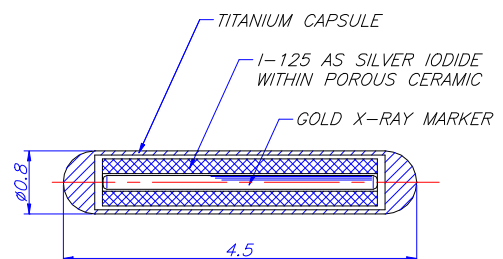
The product was certified in accordance with Directive 90/385/EEC for active medical devices, which can be implanted. The licence to attach the CE mark was issued in 1999.

IsoSeeds[®] I-125 are intended for single use. They are supplied in a sterile form. Information on the sterilisation procedure can be found in section 12.

The application of the IsoSeeds[®] I-125 according to these instructions is limited to brachytherapy of prostate carcinoma (see section 10). For the implantation of IsoSeeds[®] I-125 additional accessories are required (see section 11).

IsoSeeds[®] I-125 are sealed radioactive sources. Each IsoSeed[®] I-125 contains a cylindrical-shaped ceramic saturated with a radioactive iodine-125 compound, which is enclosed by a laser-sealed titanium tube. Gold wire inside the ceramic is used as an X-ray marker.

Iodine-125 isotope has a half-life of 59.46 days. It decays as a result of electron capture by the radiation of X-rays and γ -radiation in the energy range up to 35 keV. The electrons emitted during this decay are absorbed by the titanium capsule material.



BEBIG IsoSeed[®] I-125

4. SPECIFICATIONS

a) Activity

The IsoSeeds[®] I-125 are supplied by the manufacturer in 26 different classes of activity. The selection of activity to be used is at the sole discretion of the physician. Resulting from manufacture the value can of course fluctuate within the classes of activity indicated in Table 1. The class of activity is given on the certificate enclosed with each delivery.

Table 1: Division of classes of activity

Classes no.	Air kerma strength in $\mu\text{Gy m}^2/\text{h}$	Apparent activity in mCi	Apparent activity in MBq
-3	0.258-0.278	0.203-0.219	7.50-8.12
-2	0.279-0.302	0.220-0.238	8.13-8.82
-1	0.303-0.328	0.239-0.258	8.83-9.56
0	0.329-0.356	0.259-0.280	9.57-10.37
1	0.357-0.386	0.281-0.304	10.38-11.26
2	0.387-0.419	0.305-0.330	11.27-12.22
3	0.420-0.455	0.331-0.358	12.23-13.26
4	0.456-0.493	0.359-0.388	13.27-14.37
5	0.494-0.535	0.389-0.421	14.38-15.59
6	0.536-0.581	0.422-0.457	15.60-16.92
7	0.582-0.630	0.458-0.496	16.93-18.37
8	0.631-0.683	0.497-0.538	18.38-19.92
9	0.684-0.742	0.539-0.584	19.93-21.62
10	0.743-0.805	0.585-0.634	21.63-23.47
11	0.806-0.874	0.635-0.688	23.48-25.47
12	0.875-0.948	0.689-0.746	25.48-27.62
13	0.949-1.028	0.747-0.809	27.63-29.95
14	1.029-1.115	0.810-0.878	29.96-32.50
15	1.116-1.210	0.879-0.953	32.51-35.27
16	1.211-1.313	0.954-1.034	35.28-38.27
17	1.314-1.425	1.035-1.122	38.28-41.53
18	1.426-1.546	1.123-1.217	41.54-45.04
19	1.547-1.678	1.218-1.321	45.05-48.89
20	1.679-1.820	1.322-1.433	48.90-53.03
21	1.821-1.975	1.434-1.555	53.04-57.55
22	1.976-2.142	1.556-1.687	57.56-62.42

The calibration of the measurement of air kerma strength is traceable to Standard $S_{K99\text{std}}$ of the National Institute of Standards and Technology, USA which became effective in 1999. IsoSeeds[®] I-125 have always been calibrated to the new Standard. The value given for the activity on the certificate always refers to apparent activity which is calculated from the measured air kerma of the IsoSeeds[®] I-125.

Each seed is measured individually and classified into the corresponding class of activity. The overall uncertainty of the measurement is better $\pm 3\%$.

b) Geometric measurements

The dimensions of the cylindrical-shaped IsoSeeds[®] I-125 are:

Length:	4.5 mm \pm 0.2 mm
External diameter:	0.8 mm \pm 0.04 mm
Wall depth of capsule material:	0.05 mm \pm 0.005 mm

c) ISO-classification and leak test

The IsoSeeds[®] I-125 were subjected to an ISO-classification test and graded in accordance with ISO 2919 and DIN 25426 Part 1 as C 63211. All sources are leak tested by immersion in a suitable liquid at 70°C for 30 min according to ISO 9978.

d) Radiochemical impurities

Radiochemical impurity of the iodine-125-solution is below 0.1%. In detail the radiochemical impurities are:

Gamma: I-126 ≤ 0.005%

Beta: Cs-134 and Cs-137 ≤ 0.001 %

e) Biocompatibility

The surface of the product consists of titanium according to ASTM F 67 which assures good biocompatibility.

3. USE BY DATE, EXPIRY DATE

The activity of the IsoSeeds[®] I-125 decreases per week by one class of activity. Using Table 2 the activity of the IsoSeeds[®] I-125 on the day of application can be calculated.

The application period for IsoSeeds[®] I-125 is limited to maximum 8 weeks after the date of manufacture.

Table 2: Table of decay for Iodine-125

Days	Decay factor	Days	Decay factor
1	0.988	15	0.839
2	0.977	16	0.830
3	0.966	17	0.820
4	0.954	18	0.811
5	0.943	19	0.801
6	0.932	20	0.792
7	0.922	21	0.783
8	0.911	28	0.721
9	0.900	35	0.665
10	0.890	42	0.613
11	0.880	49	0.565
12	0.869	56	0.520
13	0.859	63	0.480
14	0.849	70	0.442

5. MANUFACTURING DATA

The precise manufacturing data and class of activity at the reference date are set out in the certificate enclosed with each delivery.

6. DETAILS ON STRUCTURE, TYPE, INTENSITY AND DISTRIBUTION OF RADIATION

Dose distribution around the source has been calculated with a Monte-Carlo-Simulation in accordance with the AAPM TG 43 protocol and verified by measurements. The AAPM TG-43 formalism is designed to calculate the dose at any point in water according

$$\dot{D}(r, \theta) = S_K \cdot \Lambda \cdot \frac{G(r, \theta)}{G(r_0, \theta_0)} \cdot F(r, \theta) \cdot g(r)$$

where

S_K	air kerma strength
Λ	dose rate constant
$G(r, \theta)$	geometry function
$F(r, \theta)$	anisotropy function
$g(r)$	radial dose function
(r_0, θ_0)	reference point, on the vector perpendicular to the source axis ($\theta_0 = \pi / 2$), 1cm from the source centre ($r_0 = 1cm$).

Air kerma strength is the measurement unit of source strength and proportional to activity.

The dose rate constant depends on the type of the source, for IsoSeeds® I-125 the dose rate constant is 1.033 cGy h⁻¹ U⁻¹.

The geometry function, the radial dose function and the anisotropy function are shown in table 3 to 5. The radial dose function can be used to calculate the dose depth distribution.

Table 3: Geometry function $G(r, \theta)$ times r^2 for IsoSeed® I-125, (approximated by 3.5 mm line source)

θ (degree)	r in cm									
	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
0	1.140	1.032	1.014	1.008	1.005	1.003	1.002	1.002	1.001	1.001
5	1.138	1.031	1.014	1.008	1.005	1.003	1.002	1.002	1.001	1.001
10	1.132	1.030	1.013	1.007	1.005	1.003	1.002	1.002	1.001	1.001
15	1.124	1.029	1.013	1.007	1.004	1.003	1.002	1.002	1.001	1.001
20	1.113	1.026	1.012	1.006	1.004	1.003	1.002	1.002	1.001	1.001
25	1.099	1.024	1.010	1.006	1.004	1.003	1.002	1.001	1.001	1.001
30	1.084	1.021	1.009	1.005	1.003	1.002	1.002	1.001	1.001	1.001
35	1.069	1.017	1.008	1.004	1.003	1.002	1.001	1.001	1.001	1.001
40	1.053	1.014	1.006	1.003	1.002	1.002	1.001	1.001	1.001	1.001
45	1.038	1.010	1.004	1.003	1.002	1.001	1.001	1.001	1.001	1.000
50	1.023	1.006	1.003	1.002	1.001	1.001	1.001	1.000	1.000	1.000
55	1.009	1.003	1.001	1.001	1.001	1.000	1.000	1.000	1.000	1.000
60	0.997	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
65	0.987	0.997	0.999	0.999	1.000	1.000	1.000	1.000	1.000	1.000
70	0.978	0.995	0.998	0.999	0.999	0.999	1.000	1.000	1.000	1.000
75	0.971	0.993	0.997	0.998	0.999	0.999	0.999	1.000	1.000	1.000
80	0.966	0.991	0.996	0.998	0.999	0.999	0.999	0.999	1.000	1.000
85	0.963	0.990	0.996	0.998	0.998	0.999	0.999	0.999	1.000	1.000
90	0.962	0.990	0.995	0.997	0.998	0.999	0.999	0.999	0.999	1.000

Table 4: Radial dose function $g(r)$ for IsoSeeds[®] I-125

r in cm	$g(r)$	r in cm	$g(r)$
0.1	1.001	3.5	0.622
0.2	1.019	4.0	0.548
0.3	1.026	4.5	0.482
0.5	1.029	5.0	0.420
0.75	1.020	6.0	0.323
1.0	1.00	7.0	0.239
1.5	0.940	8.0	0.182
2.0	0.859	9.0	0.133
2.5	0.780	10.0	0.100
3.0	0.700	11.0	0.072

Table 5: Anisotropy function $F(r,\theta)$, where r corresponds to the distance from the source centre and θ to the angle with respect to source longitudinal axis.

r in cm							
θ in degree	0.25	0.5	1.0	2.0	3.0	5.0	7.0
0	0.302	0.429	0.512	0.579	0.610	0.649	0.684
1	0.309	0.427	0.508	0.577	0.610	0.651	0.680
2	0.325	0.423	0.506	0.580	0.614	0.652	0.682
3	0.334	0.422	0.510	0.580	0.612	0.649	0.684
5	0.352	0.436	0.509	0.576	0.610	0.651	0.689
7	0.379	0.443	0.516	0.587	0.620	0.660	0.701
10	0.440	0.476	0.557	0.622	0.651	0.689	0.721
12	0.495	0.519	0.592	0.651	0.678	0.716	0.738
15	0.605	0.587	0.644	0.694	0.716	0.747	0.765
20	0.746	0.686	0.721	0.757	0.771	0.790	0.807
25	0.831	0.764	0.781	0.807	0.816	0.831	0.839
30	0.886	0.820	0.828	0.846	0.857	0.867	0.874
35	0.921	0.863	0.868	0.881	0.887	0.898	0.898
40	0.943	0.897	0.898	0.907	0.908	0.918	0.912
45	0.957	0.924	0.922	0.929	0.928	0.931	0.927
50	0.969	0.946	0.942	0.947	0.944	0.949	0.946
55	0.978	0.963	0.957	0.960	0.958	0.962	0.960
60	0.984	0.974	0.970	0.974	0.967	0.967	0.976
65	0.990	0.984	0.982	0.981	0.978	0.975	0.986
70	0.994	0.989	0.988	0.990	0.984	0.987	0.994
75	0.996	0.994	0.995	0.995	0.991	0.986	1.003
80	0.998	0.998	0.998	1.000	0.994	0.993	0.999
85	1.000	1.000	0.998	1.001	0.995	0.995	1.004
90	1.000	1.000	1.000	1.000	1.000	1.000	1.000
$\Phi(r)$	1.122	0.968	0.939	0.939	0.938	0.941	0.949

The anisotropy constant for distances ≥ 1 cm (weighted with $1/r^2$) is 0.939 .

7. RADIATION PROTECTION

The hospital in which the treatment is carried out, must have a licence for handling radioactive substances, in particular the nuclide Iodine-125 and must submit to the supplier the form according to Euratom regulation 1493/93. **Only authorised, specialised staff trained in handling radioactive substances according to the regulations on radiation protection may handle the IsoSeeds[®] I-125.** Personal dose meters must be used for checking the exposure of staff to radiation.

Suitable protective shielding must be used for storage and handling of the IsoSeeds[®] I-125. Lead foil with a thickness of 0.8 mm is sufficient for protection. In contrast, materials of low nuclear charge (e.g. plastics or aluminium) are not suitable for protective shielding. If free handling should be necessary, short exposure time and maximum distance from the source of radiation should be observed. **Direct contact with the IsoSeeds[®] I-125 must be avoided.** Preloaded magazines should only be touched on the hexagonal head for short a time and as far away from the seeds as possible. Tweezers have to be used to handle loose seeds.

After treatment the exposure rate at skin surface of the patient and at 1 meter distance has to be measured. The operating room has to be surveyed for remaining radiation sources.

The IsoSeeds[®] I-125 must be handled carefully. **Improper handling can involve the risk of radioactive contamination for the patient and the surroundings.** The IsoSeeds[®] I-125 must not be handled with sharp or pointed objects. Scratching or other damage to the surface and deformation of the IsoSeeds[®] I-125 must be avoided.

Deformed seed could leak. In the event of a seed being deformed, the immediate area must be checked for contamination. Wipe tests according to ISO 9978 are suitable for this purpose. The damaged seed has to be disposed of in a leakproof container according to the regulations of the hospital (see also section 13 and 14).

8. UNPACKING

The IsoSeeds[®] I-125 are dispatched in type A standard packaging. As a standard up to 15 IsoSeeds[®] I-125 are packed in each Mick[®]-Magazine placed in a radiation protection capsule made of stainless steel. The Mick[®]-Magazines are intended for single use. On request the IsoSeeds[®] I-125 are also available as loose seeds packed in a radiation capsule without the magazine. Several of these radiation protection capsules, each sealed in sterilisation foil, are packed in foam plastic. (See also packing drawings in section 19).

On receipt, the packet and the inner packaging must be checked for damage, correct labelling and completeness of the content. In the event of damage to the packet or the inner packaging, the IsoSeeds[®] I-125 must not be used. The packet or inner packaging must be stored in a safe place with radiation protection. Please consult the manufacturer who will advise you on the further course of action.

Please inform the manufacturer of missing labels and incorrect details on the labels and the certificate. The IsoSeeds[®] I-125 shall only be used after consultation with and the approval of the manufacturer

For unpacking open the cardboard box and remove the polysterene top. Underneath are the sterile bags with the radiation protection capsules between layers of foam plastic. The radiation protection capsules shield most of the radiation. However removal and handling shall always be done in a planned and most efficient manner.

Please check that the sterile bag has not been damaged. In the event of damage to the sterile packaging, the sterility of the radiation protection capsule containing the IsoSeeds[®] I-125 is no longer guaranteed. IsoSeeds[®] I-125 taken from damaged sterile packaging shall not be used without re-sterilisation. They can be re-sterilised using the procedure specified by the manufacturer in section 12.

The sterile packaging shall only be opened under sterile conditions. Open the package by tearing the packaging on the end indicated on the sterile bag. When opening the radiation protection capsule of loose IsoSeeds[®] I-125, assure that the capsule is in a upright position so that the IsoSeeds[®] I-125 cannot fall out of the capsule. When taking out loose IsoSeeds[®] I-125 or magazines the preservation of their sterility and sufficient shielding has to be ensured (see section 7).

9. STORAGE AND INTERNAL TRANSPORT

Storage of the IsoSeeds[®] I-125 has to be in an area providing adequate radiation protection and preventing unauthorised access, in accordance with the regulations of radionuclide laboratories. Fire protection measures must conform to the statutory regulations for radionuclide laboratories.

It is recommended to use the radiation protection capsule of the original packaging for storage and internal transport. The IsoSeeds[®] I-125 must not be brought into contact with concentrated acid or alkaline solutions. Contact with hydrogen chloride must likewise be avoided.

10. APPLICATION INDICATIONS

Indications

The IsoSeeds[®] I-125 are used for interstitial seed implantation therapy of localised tumours, especially in the prostate.

Contraindications

Treatment of tumours in a generally bad or ulcerated state is not recommended.

Adverse reactions

Since the therapeutic effect is achieved by radioactive radiation, radiation damage can occur in healthy tissue.

Possible adverse reactions associated with implant usage in the prostate have been reported to include irritative uropathy symptoms including increased urinary frequency, urgency and obstruction. Complications have also included cystitis, urethritis, superficial urethral necrosis, hematuria, stricture and contracture, impotence, incontinence and proctitis.

Implantation

Implantation of the IsoSeeds[®] I-125 shall only be carried out by appropriately trained medical experts trained for brachytherapy. Adequate training and advice on brachytherapy is provided by BEBIG.

To ensure medical quality standards, several recommendations for brachytherapy with permanent implants have been issued. The references indicated in section 18 are only a selection of main publications and do not in any case replace practical training.

Radiation planning

Planning for radiation shall only be carried out by qualified and licensed specialised staff. The initial dose rate of an IsoSeed[®] I-125 depends on the prescribed total dose. The desired

distribution of dose is achieved by the appropriate number and arrangement of the IsoSeeds[®] I-125 in the tissue.

For the calculation of the total dose distribution, the slight anisotropy of each seed should be accounted for. This feature is typical for seeds due to construction particularities (see table 5).

Checking positioning of the IsoSeeds® I-125

The IsoSeeds® I-125 must be positioned accurately at the established point within the prostate for effective treatment. Positioning has to be checked continuously during the implant procedure. Checking correct positioning of the IsoSeeds® I-125 can be carried out with the aid of ultrasound and fluoroscopy. The full length gold X-ray marker of the IsoSeed® I-125 provides for good visibility.

11. ACCESSORIES

Prior to surgery it is imperative that the instrumentation is in proper operating condition and that all components are accounted for. Essential accessories for brachytherapy are the seeds, implantation needles, a stepper with stand, a template and the planning software. The accurate positioning of the seeds has to be checked by appropriate methods, ie ultrasound, which can be combined with fluoroscopy or CT. For the applicator technique an applicator, seeds in magazines and special implantation needles for the applicator technique are required. For handling loose seeds or in case a reloading is necessary reverse action tweezers or reverse action tweezers and a V-Block respectively are recommended.

All above mentioned devices and accessories can be obtained from BEBIG. Please contact BEBIG customer support for more information. Only accessories which are CE marked and approved by BEBIG should be used. BEBIG guarantees the compatibility of BEBIG IsoSeeds I-125, the Mick®-Magazines and the Mick® 200-TPV Applicator as well as the implantation needles distributed by BEBIG.

Mick®-Magazine

As a standard the IsoSeeds® I-125 are supplied sterile in Mick®-Magazines, which are suitable for use in combination with the Mick® 200-TPV Applicator. Mick®-Magazines are intended for single use. The magazine consists of a hex head with plunger and the seed cartridge which contains the IsoSeeds® I-125. When handling the magazine adequate radiation protection has to be ensured.

For the use of the Mick®-Magazines as accessory to the Mick® Applicator, please consult the instructions for use of the Mick®-Applicator. The Magazines have to be inserted in the magazine receptor, seeds facing to the right. Before inserting check that the sterile packaging has not been damaged and the seeds are straight and parallel.

If the seeds are used loose, unscrew the seed-cartridge from the hex head. The user is entirely responsible for maintaining sterility or resterilisation.

In rare cases reloading might be necessary e.g. if seeds become blocked in the cartridge. Should this occur the following procedure using a loading block and reverse tweezers is recommended. Stabilize the cartridge in the seed loading V-Block and unscrew the hex head. Remove the blocked seeds and reload using the reverse action tweezers. Reinsert plunger paddles into cartridge groove, apply downward pressure and thread hex-head onto cartridge until tight. This procedure should only be conducted behind a protective shield. Wearing lead-lined gloves significantly reduces exposure to fingers and hands.

Mick®-Applicator

The Mick® 200-TPV Applicator is suitable for use in conjunction with the IsoSeeds® I-125, the Mick®-Magazines and the implantation needles designated in the following paragraph. The applicator can be obtained from BEBIG GmbH.

Implantation needle

Special 17-gauge (1.4 mm, normal) or 18-gauge seed (1.2 mm, extra thin) implantation needles are to be used for the implantation of IsoSeeds® I-125. Implantation needles are available from BEBIG GmbH.

For the Mick applicator technique implantation needles that are suitable for the Mick® 200-TPV Applicator have to be used. BEBIG declines any responsibility for the compatibility of needles that have not been provided or recommended by BEBIG. In case seed implantation needles not recommended by BEBIG are used, it has to be checked before treatment that the needle fits well into the applicator needle holder and that a firm grip is ensured.

The exact description of the accessory products referred to above and their use can be found in the respective instructions for use enclosed. Flawless function of IsoSeeds® I-125 is only assured if the instructions for use of the accessories are observed and the function of the accessories is assured.

12. STERILISATION

The IsoSeeds® I-125 are supplied in sterile condition. For sterilisation steam sterilisation at 121 °C is used for 15 min in accordance with DIN EN 554 and DIN EN 285. The IsoSeeds® I-125 are sterilised together with the Mick®-Magazine, the radiation protection capsule and the sterile packaging. In case of loose seeds the magazine is omitted.

If re-sterilisation of the IsoSeeds® I-125 should be necessary, e.g. if the sterile packaging was damaged, the validated procedure used by the manufacturer must be used. To clean the IsoSeeds® I-125 before re-sterilisation alcohol, acetone or mild detergent can be used. The manufacturer declines any liability for the sterility in case of re-sterilisation. Sterilisation time should be extended to 30 min. Resterilisation may weaken the plastic components of the Mick®-Magazines. The IsoSeeds® I-125 must not be exposed to temperatures above 130° C.

13. WARNINGS, SAFETY MEASURES

Safety measures in the hospital

The radiation protection regulations for the operation of radionuclide laboratories must be complied with. The user, i.e. the hospital, must introduce suitable safety measures to avoid incidents, and draw up and maintain emergency plans. The following instances should be taken into account especially for handling the IsoSeeds® I-125:

a) Damage or contamination of the IsoSeed® I-125

Radioactive Iodine-125 cannot escape from the IsoSeed® I-125 under normal circumstances. **Should leakage or contamination be discovered, however, the damaged IsoSeed® I-125 must be excluded from further use immediately and the radiation safety officer notified.** All seeds or equipment which have been in contact with the damaged seed have to be checked and cleaned. The surrounding areas must be closed off. Persons involved must be checked for contamination. After the damaged IsoSeed® I-125 has been transferred to a lockable radiation protection container and the area has been decontaminated the access to the surrounding areas can be allowed again by the radiation safety officer.

b) Loss of an IsoSeed® I-125

Because of its small size an IsoSeed® I-125 can get lost as a result of improper or careless handling. In this case the immediate area must be closed off immediately. Access cannot be allowed until the seed is found. For detection of the lost seed a dose meter should be used.

Patient education

The doctor carrying out the treatment or the hospital must inform the patient and his next of kin about the type of treatment, the accompanying risks and the requisite protective measures. In particular, he shall inform the patient about certain protective measures mentioned in the following paragraphs:

a) Excretion of an IsoSeed® I-125

The patient has to be advised of the possibility that an IsoSeed® I-125 might be excreted in rare cases. The patient must be instructed on correct handling of the IsoSeed® I-125 in the event of an IsoSeed® I-125 being excreted. The doctor in charge or the hospital has to be informed as soon as possible. Direct contact with the seed must be avoided. The IsoSeed® I-125 can be picked up using tweezers or a spoon and locked in a suitable container, e.g. made of glass, which should be stored in an inaccessible place as far away from living areas as possible until the doctor in charge or the hospital arranges for further steps. During two months following the implant the patient should use condoms for intercourse.

b) Risk to others from the patient

To keep the radiation exposure of family members and other contacts as low as possible, extended body contact, i.e. more than a few minutes per day up to 8 weeks after the implantation should be avoided. Pregnant women and children under 18 years of age should keep a safety distance of approx. 2 meters from the patient during this period.

c) Death of a patient

In the event of the death of the patient within 2 years after implantation of the IsoSeed® I-125, the relatives are obliged to consult the doctor in charge or the authorities responsible for radiation protection at the hospital with respect to the burial modalities. In the event of the death of the patient after this period, no special safety measures are required.

14. DISPOSAL

Disposal of the IsoSeed® I-125 is carried out in compliance with the regulations laid down by the hospital concerned, which must conform to the rulings of the respective supervisory authority.

Disposal of the IsoSeed® I-125 is necessary in the following instances:

- a) Damage to or contamination of the IsoSeed® I-125 occurs. (see section 13). For seeds that may not be leaktight particular regulations may have to be observed. In any case these seeds have to be disposed only in tight containers according to the regulations of the hospital.
- b) There are IsoSeeds® I-125 left over which have passed the expiry date. The expiry date can be found at the certificate or on the sterile packaging.
- c) The IsoSeeds® I-125 are excreted by the patient (see section 13).

15. SAFETY PROCEDURE IN CASE OF ANY UNCERTAINTY

Should you notice anything unusual about the IsoSeed® I-125, or if you have any other questions about the product, please contact the manufacturer immediately. For fast processing please fax your question together with a copy of the certificate and the telephone number and fax number of a contact.

16. OBLIGATION TO ADVISE OF ANY COMPLICATIONS

According to European and German law we are obliged to report any incident with our products to the German authorities. The obligation to report is based on article 8 of directive 90/385/EEC for active implantable medical devices as well as §§ 29-31 of the German law on medical devices.

Therefore, we would like to ask you to inform us immediately about any incident occurring in connection with the use of our products, in particular:

- side effects
- reciprocal influences with other substances or products
- malfunctions
- technical faults
- contraindications
- adulteration
- any hazards

We are also eager to hear about any suggestions for improvements of our products.

17. CUSTOMER SUPPORT

Our recommended brachytherapy method implies the use of the Mick-Applicator and the magazines loaded with BEBIG IsoSeeds® I-125. To ensure compatibility of all components used for the treatment please contact the customer service of BEBIG. BEBIG offers ongoing training and expert advice on all areas of brachytherapy. All materials and equipment requirements are discussed during individual training sessions and any necessary items can be obtained through BEBIG.

To order the above mentioned devices and accessories as well as for information about training on brachytherapy please contact:

Customer Service for Brachytherapy Products

BEBIG Isotopen- und Medizintechnik GmbH
Robert-Rössle-Straße 10 D – 13125 Berlin

Phone.: (+49 30) 94 10 84-130
Fax: : (+49 30) 94 10 84-112

18. REFERENCES

Recommendations

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S. Smathers, K. Wallner, T. Korssjoen, C. Bergsagel, R. H. Hudson, S. Sutlief, J. Blasko, Radiation Safety Parameters Following Prostate Brachytherapy, *Int. J. Oncology Biol. Phys.*, Vol. 45, No. 2, 397-399, 1999.

**19 PACKAGING DRAWING:
ISOSEEDS I-125 IN MAGAZINE (STERILE), ISOSEEDS I-125
(LOOSE, STERILE)**

