Preparation of a prototype radioactive probe for treatment of lacrimal ducts stenosis and a study of its dose distribution

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Abstract

Our aim was to prepare a radioactive lacrimal passages probe, study its dose distribution in a phantom and suggest security indexes and therapeutic effective doses for brachytherapy. *We prepared* the radioactive probes by laying ^{125}I particles into plastic tubes. We conducted temperature tests, pressure tests, soak tests and shock tests, to obtain security indexes. The dose distributions in phantom and wax matrix were also detected, and the surface dose rates on different parts of the phantom and the dose absorbed by the operator were examined. *The radioactive lacrimal passage probe demonstrated* no form changes in temperature tests, pressure tests and soak tests when using a surface radioactive contamination dose lower than 185Bq. The probe was waferinged in shock tests with a surface radioactive contamination dose lower than 185Bq. The dose detection in the phantom and the wax matrix showed that for distances of 1mm-12mm off the tube, there were statistical differences of the absorbed dose ($P<0.05$). However, for the range of 12mm-40mm, there was no statistical difference ($P>0.05$). The dose rates administered by the radioactive probe used for radiotherapy to the lacrimal passages were within safe limits both for the phantom (Sichuan Keyi Corporation, China) and the operator. *In conclusion*, our study showed that this prototype lacrimal passages probe can be a useful and effective method for clinical brachytherapy of lacrimal ducts stenosis.

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Introduction

Stenosis of lacrimal passages is one of the common diseases in ophthalmology for senior people. Treatment through probing of the lacrimal passages has been proved so far ideal for the expectation of short and long-term effects [1-3]. Consequently, seeking for a safe and less traumatic novel strategy has become a research focus of this field. In this paper, we studied the preparation of an up-to date radioactive probe using iodine-125 (^{125}I) as the radionuclide. The dose distribution, the effectiveness and feasibility of this radioactive probe treatment for lacrimal duct stenosis has been studied.

Materials and methods

Equivalent model and ^{125}I radioactive seeds

An equivalent phantom was purchased from Sichuan Keyi Corporation, China. A 10X10X10cm cubic cavity block was prepared. Melted paraffin wax was poured into this block to make paraffin wax patrix. A sealed titanium and titanium alloy ^{125}I radioactive seed, produced with the assistance of China Institute of Atomic Energy, was filled with ^{125}I. This seed was 0.80±0.02mm wide, 4.50±0.20mm long and had a 0.30±0.05mm wall thickness [Fig. 1]. All seeds were qualified through regular tests in their appearance, component, possible surface radioactive contamination, etc.

Animals and equipments

Ten inbred strain white rabbits were purchased from Laboratory Animal Department of Jilin University, China. Dose Rate Detector DH3103A (Beijing Nuclear Instruments Factory), Radioactivity Detector IGC-7 (TOSHIBA Corp., Japan) and Thermoluminescent Detector FJ377 (Beijing Nuclear Instruments Factory, China) were used.

Preparation of lacrimal passage probe

The ^{125}I seeds were placed linearly into the medical application tube heated for contraction to be better fixed and then the tube was sealed to form the probe. The seeds

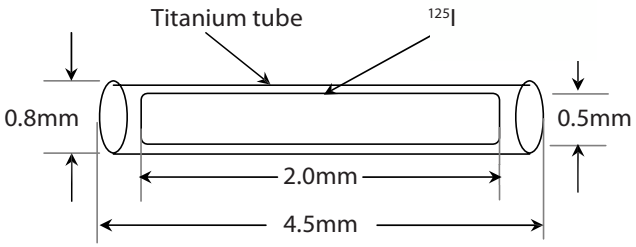

Figure 1. The stuctrure of the ^{125}I seed which was produced by China Institute of Atomic Energy.

quantity in a probe depended on the estimated length of the lacrimal duct stenosis. Radioactivity of each probe was detected after its formation was completed. A serial of primary tests were practiced, including temperature test which maintains -40~+105°C for 60min, pressure test which keeps 25kPa for 25min, soak test which keeps the probe in sterilizing liquid for 10h and shock test which keeps the probe in a flat steel plate to receive the hit of a 50kg hammer, freely falling from 1m height. The probe appearance and surface radioactive contamination were also noted.

Dose distribution of the probe in paraffin wax model and phantom

A flour of LiF was used. LiF is an element of thermoluminescence detector. It is mainly made up of Magnesium (Mg, 0.1mol%), Copper (Cu, 0.004mol%) and Phosphonium (P, 0.5mol%) was annealed at 240°C. After cooling on the aluminum plate, 20mg LiF flour was placed within 2mmX20mm plastic tubes sealed and kept in a lead castle. The ^{125}I probe, was placed in the center of the paraffin wax model, and the LiF detecting apparatus was set at distances of: 1mm, 2mm, 3mm, 4mm, 5mm, 6mm, 7mm, 8mm, 9mm, 10mm, 11mm, 12mm, 13mm, 20mm, 30mm and 40mm off the probe, in directions of the six planes of the cubic model. As for the phantom, two probes were inserted in the nasolacrimal ducts, and the LiF detecting apparatus was set at the above: 1mm to 40mm mentioned sites posteriorly to the probe. The detecting apparatus was also set anterior to the probe in sites equivalent to the skin. The duration of exposure depended on the ^{125}I probe radioactivity, using a pre-determined strategy. Then the irradiated elements were removed and each sample absorbed dose was calculated ten times through a thermolumin escence detector according to the conventional method. In order to minimize measurement errors, the average double-sample absorbed doses and background dose of blank tube were also viewed.

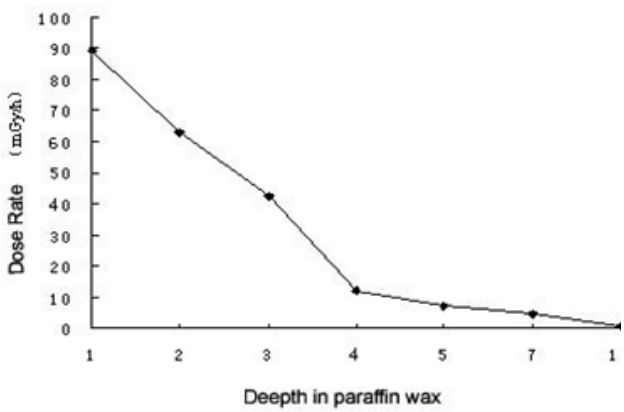

Figure 2. The dose rate-depth curve in paraffin wax

Radiation dose equivalence

Surface dose rates in different parts of the phantom and on the operator were detected. The average operation duration was recorded through manipulating the lacrimal passages of 10 rabbits. Then, the radiation dose equivalent at various sites of the phantom during a theoretical operation time was calculated. The process of these calculations was executed by the Radiation Protection and Surveillance Institute of China Health Ministry.

Statistical analysis

All data were analyzed with Student's t test through SPSS10.0 software.

Results

Results of the primary tests

The radioactive lacrimal passage probe showed no form changes in temperature, pressure and soak tests, using a surface radioactive contamination dose lower than 185Bq. However, the probe was waferinged in shock tests, with a surface radioactive contamination dose lower than 185Bq.

Table 1. *Lacrimal passage probe dose distribution, in the phantom (x=mean±SD)**

Distance(mm)	Dose rate (mGy/h)	Distance (mm)	Dose rate (mGy/h)
1.0	89.24±12.57	9.0	1.99±0.31
2.0	62.94±10.74	10.0	1.38±0.22
3.0	42.45±5.41	11.0	1.04±0.21
4.0	15.48±2.32	12.0*	0.73±0.19
5.0	11.96±1.38	13.0	0.37±0.21
6.0	7.16±0.55	20.0	0.16±0.01
7.0	4.59±0.66	30.0	0.15±0.01
8.0	3.67±0.44	40.0**	0. 13±0.01

*P<0.05, **P>0.05

Dose distribution detection

The dose detected in the phantom and the wax matrix showed that during distances from 1-12mm off the tube, the absorbed dose (AD) changes had statistical significances as the distance increased each time by 1mm (P<0.05). However, during distances from 12mm-40mm, the differences of the absorbed doses were not significant (P>0.05) [Table 1, Fig. 2].

Radiation dose equivalent

In the nasal cavity, tissues peripheral to the probe receive a

dose equivalent of about 0.38mSv. The average dose equivalent for the crystalline humor was 5.12μSv, while for the heart, lung and the brain was under 0.5μSv. Animal experiments demonstrated that the average irradiation time for one lacrimal passage is about 7min. Consequently, the operator will receive an average dose equivalent of about 5.0μSv.

Discussion

Lacrimal ducts contain two histological components, the epithelial layer and the stromal layer. The epithelial layer is composed of two kinds of cells, the upper, columnar cells, and the deeper, pavement cells, with beaker cells included in this layer. The stromal layer has an upper gland-like layer with lymphocytes, to connect with the epithelial layer. The base of the lacrimal ducts is a fibrous connective tissue layer with fibroblasts. The occurrence of lacrimal duct stenosis will stimulate fibroblasts and epithelial cells to proliferate at high levels. Currently, the lacrimal duct probing treatment has certain therapeutic effects in clinical practice. However, most patients suffer restenosis several months after treatment [4, 5]. Radiation has distinct inhibitory effects on cell proliferation, which have been proved in basic research studies and verified through clinical applications, for cutaneous hemangioma, for coronary artery restenosis, for post-percutaneous transluminal coronary angioplasty, for benign prostatic hyperplasia etc. [6-8]. The satisfactory effect of radiation treatment of the above clinical applications indicates a potential application of the radioactive lacrimal passage probe.

Previous research has shown that an absorbed dose over 10Gy will be enough to destroy gene transcription or directly damage the cell membrane's integrity [9]. Pathological research demonstrated that the average thickness of stenosis in lacrimal passage is 2-4mm. The radioactive probe dose distribution results show that 85% of irradiation energy has been emitted at a distance of 5-6mm from the probe and will release enough energy to the stenotic tissues in a very short time.

The radioactive probe has an appearance identical to a common probe and has combined favorable behavior in mechanical probing and for radiation treatment. Gamma rays radiation level in paraffin wax model is almost equal to background at a distance of 20mm. Plastic tubes used in medicine have no side effects [10], but the plastic radioactive probe was deformed in the shock test, although without radionuclide contamination. Better physical properties should guarantee that the radioactive probe is safe both for application and storage.

According to the kind of radiation emitted, the stenosis extent, the sensitivity of the peripheral tissue and most important, according to the national dose limits, the radiation dose for pathological tissues was determined as 7-8Gy. Under these circumstances, as already mentioned, tissues peripheral to the probe will accept a dose equivalent lower than 0.5mSv, the crystalline humor a dose lower than 10μSv and the heart, lung and the brain a dose lower than 0.5μSv. Animal experiments demonstrated that for completing irradiation treatment to one lacrimal passage about 7min would be enough. Under this operation standard, consequently, the operator will get an average dose equivalent of about 5.0μSv, about 1% lower than the upper limit acknowledged by the International Commission of Radiological Protection (ICRP) [11, 12]. Suppose the operator applies 3 such treatments in one day and works 200 days in a year, he will receive a dose equivalent under 5mSv.a^{-1}, which is only 10% of the allowed professional dose equivalent (50mSv.a^{-1}) [13]. Thus, for a skilled practitioner, the application of the radioactive lacrimal passage probe will be safe both for him and for his patients.

In conclusion, the prototype radioactive lacrimal passage probe that we suggest for branchytherapy can be applied in lacrimal duct stenosis as a new and safe treatment strategy.

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The authors declare that they have no conflicts of interest.

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Experimental study on a new radioactive probe for the treatment of lacrimal duct stenosis

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Abstract

Our aim was to study the treatment effect of a radioactive probe on lacrimal duct stenosis. *We applied* experimentally in 30 inbred white rabbits a lacrimal duct stenosis model and the rabbits were randomly divided into 3 groups: the stenosis group, the surgery group and the radioactive probe group. We also separated a blank control group of 5 rabbits. Rabbits in the surgery group and the radioactive probe group were examined by digital subtraction angiography (DSA) 10min and 30d after treatment before being sacrificed. Rabbits in the stenosis group and the control group were examined by DSA 60min before they were sacrificed. Specimens of the lacrimal ducts at the stenosis site were collected immediately after the rabbits were sacrificed. Morphological changes were observed through haematoxyline-eosin staining, while lumen areas of lacrimal duct were observed through computer based photo analysis. *For the surgery and the radioactive probe group*, stenosis cure rates were 100% 10min after treatment. Thirty days after treatment, the rates of stenosis were 40% and 5% for the above groups, respectively. Morphological observations showed that each layer of the lacrimal duct wall in the stenosis group became thicker with higher proliferation of cells. Each layer of the lacrimal duct wall in the surgery group was thinner than in the stenosis group; however, the extent of cell profileration was similar. In the radiation treatment group, the interstitial layers of the lacrimal duct epithelium, elastin and collagen fibers and other connective tissue components were thinner than in the surgery group. Cells proliferation was significantly weakened in the radiation treatment than in the stenosis and in the surgery groups. The average areas of lacrimal duct in the control, stenosis, surgery and the radioactive probe groups of the examined sites, were: 0.84±0.28mm^2, 0.26±0.13mm^2, 0.55±0.31mm^2 and 0.80±0.36mm^2, respectively. *In conclusion*, the radioactive lacrimal duct probe showed distinct therapeutic effects in curing lacrimal duct stenosis and in preventing restenosis after the operation.

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Introduction

Lacrimal duct or passage stenosis is a common ophthalmic disease and accounts for 3% of all visits to ophthalmologists [1]. Surgery is widely used to treat this disease. However, most of the patients experience a re-stenosis 2-4 weeks after treatment, which greatly affects the clinical outcome [2]. Previously, we had designed a new radioactive lacrimal duct probe using radionuclide ^{125}I [3]. We concluded that the use of this probe was safe and could also provide long term effects in probing stenosis. In the present study, we compare the treatment effect of this new radioactive probe with the traditional lacrimal duct surgery, to further evaluate its treatment effect on lacrimal duct stenosis.

Animals and methods

We obtained from the experimental animal department of Jilin University 45 inbred white rabbits with weight 2.5±0.5kg, age 8-12 weeks, either male or female. DH3103A Dose Rate Detector (Beijing Nuclear Instruments Factory) and radioactivity detector (TOSHIBA Corp., Japan) were used to measure the distribution characteristics of dosimetry of ^{125}I. We used an optical microscope, (BX41-72H02, Olympus, Japan) and for digital subtraction angiography (DSA) we used a 1250MA angiographer from Shimadiu Japan. Computer image analysis system was performed by HPIAS-100, Tongji China. Forty inbred white rabbits were randomly chosen and detected by DSA for lacrimal duct patency. Bilateral lacrimal duct stenosis models were prepared using probes with