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[Reprinted from RADIOLOGY, Vol. 63, No. 3, Pages 390–99, September, 1954.]
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Radiogold Seeds in Clinical Radiation Therapy[1]

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During the first year of application of seeds containing radioactive gold 198 (1–7) in clinical radiation therapy at the Ohio State University Medical Center, 100 patients were treated with the new types of gamma-ray sources. Although insufficient time has elapsed for a definitive evaluation of clinical results, it is felt that enough experience has been accumulated to warrant a review of the place of radiogold seeds in the practice of radiation therapy.

No appreciable differences have been noted clinically in the reactions to therapy with radiogold, radiocobalt, radium, and radon. Radiogold seeds were found to be convenient replacements for the radon seeds formerly employed at this center. The simplicity of protection and the ease and speed of preparation of radiogold seeds of uniform strength were valuable in many situations.

Whether radiogold seeds should be used in preference to needles or nylon applicators containing radiocobalt or radium will depend largely on the clinical situation. For example, in tumors of the bladder or the gastrointestinal tract, the permanent implantation of radiogold seeds will often be preferable to the use of needles that must subsequently be removed because of the long-lived gamma-ray emitters they contain. Important uses for radiogold seeds will also be found where a large number of patients have to be treated on an out-patient basis because of the paucity of hospital beds.

Four methods of application of radiogold sources were used: (1) molds; (2) intracavitary applicators; (3) permanent implants; (4) removable nylon implants.

RADIOGOLD SEEDS IN MOLDS

Molds with radiogold seeds were employed in 2 of the first 100 patients. One patient had a carcinoma of the skin and the other had a carcinoma of the floor of the mouth.

The long-lived radioisotopes, such as radiocobalt and radium, are the usual choice for molds, because no extra expense or labor is required in preparing these radioactive substances if they are available in the hospital. However, molds containing radiogold sometimes offer advantages over other gamma-ray emitters: (*a*) the necessity of hospitalization or repeated visits is obviated; (*b*) adjacent radiosensitive tissues can be protected effectively with lead shields; (*c*) recovery of the radioactive substances from the molds is not required.

(*a*) *Use of radiogold seeds in molds to avoid hospitalization or repeated visits* is occasionally valuable in elderly patients with small skin carcinomas who live far from the hospital. This method of treatment requires but a single visit to the radiotherapeutic center for the preparation and application of the mold. Subsequent removal of the mold and follow-up can be carried out by the physician who refers the patient.

For this type of application, radiogold seeds offer no essential advantages over radon seeds used in a similar manner. Occasionally, the immediate availability of the radiogold seeds may save a patient an extra trip, which may be required if radon seeds have to be ordered. The risk of

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Presented at the Thirty-ninth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 13–18, 1953.

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accidental loss makes the use of long-lived radioisotopes, such as radiocobalt or radium, undesirable for this purpose.

(*b*) *Effective protection of adjacent tissues by a lead shield* is a second reason for the occasional use of radiogold seeds in molds. The incorporation of lead in molds loaded with radiocobalt, radium, or radon seeds is not very effective, because the first half-value layer in lead is approximately 7.9 mm. for radium and radon filtered with 0.5 mm. platinum or gold and approximately 10.4 mm. for radiocobalt. In contrast, the half-value layer in lead for the gamma radiation from radiogold is only 2.7 mm. A lead shield of this thickness can usually be easily incorporated in the mold.

(*c*) *Elimination of the necessity of recovering the radioactive substances from the mold* after treatment is a third reason for the preference for radiogold seeds in some cases. Radiogold molds are simply discarded after use, while considerable labor and exposure to radiation may be involved in recovery of long-lived radioactive materials from molds.

In only one of the first 100 patients was there an opportunity to utilize all the advantages listed above:

CASE I: The patient was a white sales clerk, 50 years old, who had noticed an irregularity on the floor of his mouth for three months. On clinical examination, an indurated area 1.5 cm. in diameter, with superficial ulceration, was found. Biopsy showed a Grade II squamous-cell carcinoma. The tumor was treated by a permanent implantation of radiogold seeds inserted through the submental skin and an intraoral mold loaded with radiogold wires. The patient had only six front teeth in his lower jaw, to which his dental prosthesis was attached. In order to protect the tooth sockets, a lead shield was incorporated in the mold, which was made from dental compound (Fig. 1). The very reliable patient, who lived sixty miles from Columbus, was treated without hospitalization or repeated visits. He took the mold home in a lead container and applied it himself according to instructions. After one week, he brought back the mold, which was then discarded. A moderate mucositis developed, and the carcinoma disappeared clinically within three weeks. At the most recent follow-up, one year after the treatment, no evidence of disease was found and no sign of radiation damage was present.

Fig. 1. Case I. Intraoral mold with radiogold wires and built-in protective lead shield combined with a permanent implant for treatment of a squamous-cell carcinoma of the floor of the mouth.

RADIOGOLD SEEDS IN INTRACAVITARY APPLICATORS

Intracavitary applicators were used in 9 of the first 100 patients. Three applications were made for carcinoma of the endometrium, and 2 each for carcinoma of the esophagus, the urinary bladder, and the urethra.

Radiocobalt or radium is the usual choice for intracavitary applicators. Here also, however, radiogold may occasionally offer advantages over other gamma-ray emitters: (*a*) Hospitalization of the patient or regular visits are not necessary; (*b*) smaller tubes can be used than with radium; (*c*) adjacent radiosensitive tissues can be protected effectively by a lead shield.

(*a*) *Use of radiogold seeds in intracavitary applicators to avoid hospitalization or repeated visits* is feasible only rarely, since most patients in whom intracavitary applicators are used require hospitalization. In the 100 cases upon which this paper is based advantage of this possibility was taken only once.

CASE II: The patient, an easy-going colored musician, 49 years old, was first seen in December 1952, with a large painful mass in the right lower jaw and difficulty in swallowing. Biopsies revealed a Grade III squamous-cell carcinoma of the esophagus with metastasis to the right mandible.

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Fig. 2. Case II. Intracavitary applicator with radiogold seeds in nylon tubing used for treatment of esophageal carcinoma, without hospitalization.

A feeding tube was inserted, and high-voltage roentgen therapy was begun. The patient failed to keep regular appointments, however, and it was decided to attempt palliation by insertion into the feeding tube of a nylon tube loaded with radioactive gold seeds over a segment 15 cm. long. This was done Dec. 8, 1952, and a second application was possible on Dec. 19 (Fig. 2). The two applications delivered approximately 5,000 r on the surface of a cylinder 2 cm. in diameter. In addition, the metastasis in the right mandible was implanted permanently with radiogold seeds. The patient also received a tumor dose of approximately 3,000 r to the esophagus and 4,000 r to the mass in the mandible by external high-voltage x-ray therapy at his irregular visits. These treatments reduced the size of the mandibular mass to about 10 per cent and relieved the difficulty in swallowing nearly completely. The patient felt happy because, as he stated, he could "eat hamburgers again." He died from general metastases, at his home, seven months after the radiogold treatment, without having experienced any further difficulty in swallowing.

(*b*) *Use of smaller tubes than is possible with radium* is a second reason for the occasional use of radiogold seeds in intracavitary applicators. Compared with radon, there is no difference, since the outside diameter of both radiogold seeds and radon seeds is 0.8 mm. Radiocobalt pieces similarly used are even better in this respect, having a diameter of only 0.5 mm. However, radiogold or radon seeds incorporated in a tube of about 2 mm. outside diameter were small enough to be introduced even into such narrow passages as the urethra constricted by massive tumor involvement. The following case is presented as an example of the use of small diameter tubes in intracavitary applicators.

CASE III: A housewife, 65 years old, gave a history of vaginal bleeding for two months. Pelvic examination revealed a large uterus with the fundus about two and a half times the normal size. A Grade IV carcinoma was found by diagnostic curettage of the uterus. The patient was first treated with external x-ray therapy, receiving 2,000 r tumor dose from two fields. This was followed, on Oct. 15, 1952, by packing the uterine cavity with polyethylene tubing containing 44 radiogold seeds, each 4 mm. in length. Polyethylene tubing is preferred to nylon tubing for this type of application, because it is much more flexible. Since the outside diameter of the polyethylene tubing is only 2 mm., no dilatation of the cervical canal was required. The radiographs in two planes in Figure 3 show the packing in the uterine cavity, with a few seeds purposely inserted in the tubing in the cervical canal. The tubing was easily removed a week later, without sedation. During this time, a dose of approximately 7,000 r was delivered to the peritoneal surface of the uterus. Six weeks after the treatment, a total hysterectomy with bilateral salpingo-oophorectomy was carried out. Careful examination of the surgical specimen by a pathologist revealed no evidence of malignant cells. The most recent check-up on this patient, approximately a year after the treatment, showed no evidence of recurrence or radiation reaction.

(*c*) *Effective protection of adjacent tissues by a lead shield* may be a third reason for preferring radiogold seeds over other gamma-ray emitters for intracavitary applicators. In our first 100 patients treated with radiogold seeds, advantage was not taken of this possibility, but vaginal ap-

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plicators with radiogold seeds and lead protection for the rectum have been used more recently.

RADIOGOLD SEEDS IN PERMANENT IMPLANTS

Permanent implants were carried out in 51 patients. Twenty-five of these, nearly half of the total, had tumors of the head or neck. Most of the cancers were in advanced stages. Nine permanent implants were carried out in the urinary tract; of this number, 7 were in tumors in the bladder. Three tumors occurred in the vagina, 1 being primary and the other 2 metastatic from carcinoma of the cervix. Two hemangiomas in adults, 2 recurrences in the skin from carcinoma of the breast, 2 recurrent carcinomas of the colon, and 1 metastasis to the skin from bronchogenic carcinoma were also implanted permanently with radiogold seeds.

For permanent implants, only short-lived radioisotopes, such as radiogold or radon, can be used. Radiogold for permanent implants has the practical advantage over radon that seeds of uniform strength can be prepared immediately, whenever the need arises. This possibility was particularly advantageous in 7 of our patients, when a non-resectable tumor was unexpectedly encountered at surgery. Usually, the cutter in these cases was brought to the operating room and the seeds were cut and calibrated within a few minutes. Advantage of the quicker preparation of radiogold seeds has also been taken in cases referred for consultation to the tumor conference, with immediate implantation following the recommendation of the conference. In this way, consultation and treatment can be carried out in a single visit, within a few hours, after which the patient is returned to the care of the referring physician.

Fig. 3. Case III. Intracavitary applicator with radiogold seeds in polyethylene tubing used for treatment of carcinoma of the endometrium.

With present implantation technic, the pattern of seed distribution in permanent implants is not as accurate as in removable needle or nylon applicator implants. For this reason, permanent implants are pre-

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ferred over removable implants only if (*a*) removable implants are difficult to insert or (*b*) only short-term palliation can be expected.

(*a*) *Use of permanent implants when insertion of removable implants is difficult* finds its most frequent application in intra-abdominal tumors. It is especially indicated for tumors in the depth of the pelvis, as carcinomas of the bladder and of the prostate. Furthermore, for abdominal tumors a removable nylon implant cannot be prepared in advance accurately, since the shape and extent of the tumor are usually uncertain. Finally, in the abdomen, the withdrawal of needles or nylon applicators may cause bleeding. Fortunately, this complication was not encountered in the 5 intra-abdominal tumors in this series which were implanted with nylon applicators; but moderately severe hemorrhage was seen in the case of a tumor in the soft palate, and slight hemorrhage in a case of a hemangioma, during removal of the nylon applicators.

CASE IV: A 28-year-old white man had multiple adenocarcinoma of the colon on the basis of multiple polyposis. A total colectomy and permanent ileostomy were carried out in June 1951 at this hospital. For a year and a half after the operation, the patient did well, but then started to lose ground. He was readmitted in May 1953, when physical and x-ray examination revealed a mass in the left lower quadrant. At operation, June 28, 1953, a firm mass, 8 cm. in diameter, was found in the mesentery of the small bowel. It involved the region of the superior mesenteric vessels and therefore could not be excised. A separate tumor implant, 1.5 cm. in diameter, was present over the promontory of the sacrum, and an isolated node, 0.5 cm. in diameter, was found in the right side of the mesentery. Enteroenterostomy was carried out about the bowel more closely involved with the tumor, and implantation with gold seeds was requested. Radiogold seeds were prepared immediately, and fifty seeds were permanently implanted into the large mass, four seeds into the tumor implant over the promontory, and one seed into the small node in the right mesentery. In Figure 4 is shown the x-ray pattern of the seed distribution.

Fig. 4. Case IV. Permanent implant with radiogold seeds used for treatment of recurrence after resection of carcinoma of the colon.

Following dismissal, the patient improved rapidly and gained 10 pounds in weight. He became free of pain and could again work full time in a steel plant. X-ray studies on a routine check-up, in November 1953, showed good regression of the mass in the area where the seeds were implanted. However, lateral to the original mass, a part of the tumor, which probably had not received enough

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radiation from the implant, had increased in size. It was therefore decided to carry out a "third look" exploration and again to implant radiogold seeds

This case indicates that good palliation can be accomplished by implantation in non-resectable carcinomas of the intestinal tract, in which radiation therapy is frequently considered not worth while. It is believed that permanent implantation might prove to be a valuable adjunct to the so-called "second-look" operations which have been suggested for more effective control of malignant tumors of the gastrointestinal tract.

(*b*) *Permanent implants when only palliation can be expected* often appear preferable to a removable implant, since no preparation is required, local anesthesia is often sufficient, implantation is more quickly carried out, no supervision of the patient during the treatment period is required, and removal is not necessary.

CASE V: A white electrician, 39 years old, had a Grade II squamous-cell carcinoma of the left lower gum in 1949, which was treated by excision and left mandibulectomy. He progressed satisfactorily until March 1953, when a right submaxillary node appeared. This was treated elsewhere with high-voltage external x-ray irradiation and a radon implant. Within two months the skin sloughed, exposing the right mandible. In July 1953 bilateral axillary masses appeared and were treated with x-rays in still another hospital. In September 1953, painful skin nodules developed in the right supraclavicular area and the patient was referred to this hospital.

Fig. 5. Case V. Permanent implant with radiogold seeds used for palliative treatment in ulcerated right supraclavicular metastases from carcinoma of the gum.

Clinical examination showed far-advanced carcinoma with widespread involvement in the neck. Since the main complaint was the painful metastatic skin nodules in the right supraclavicular region, it was decided to attempt palliation by insertion of a permanent radiogold implant. This was done, and the patient returned immediately to his home, 120 miles from Columbus. A fair pattern in the implanted region is shown in Figure 5. A month later, the supraclavicular nodules had shrunk and there was complete relief of pain in this area. However, new subcutaneous metastases had developed in the occipital region and in the right chest wall. Implantation was carried out in these areas, and the patient returned home immediately. Because of the widespread involvement, it was expected that he would live only a few weeks. However, in a letter written eight weeks after the second implantation, he stated that "the lumps where you put the seeds in have gone away." He added that new "lumps" had appeared on the

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other side of the neck and requested another appointment for treatment.

Although there has been considerable experience with implants of radon seeds here, it is difficult to evaluate a possible difference in therapeutic effect between radiogold seeds and radon seeds implanted permanently, since the variation in pattern is so great and the accuracy of implantation is the decisive factor. Appreciable differences have not been observed clinically.

RADIOGOLD SEEDS IN REMOVABLE NYLON IMPLANTS

Implantation with removable nylon applicators was carried out in 38 of the first 100 patients. Nineteen had tumors of the head and neck. Seven were referred for treatment of hemangiomas. Three had tumors primary in the bladder, and 3 recurrent carcinomas of the cervix. In 3 advanced breast tumors, implantation of the internal mammary chain was carried out by threading nylon applicators under the sternum. A recurrent carcinoma of the colon, a carcinoma of the skin, and a retinoblastoma, which occurred after x-ray therapy, were also treated.

Preparation of the nylon applicators requires time and skill. Furthermore, the technic of preparing these applicators to carry radiogold seeds is still in the developmental stage. It is possible to use nylon tubing in a manner similar to that developed for the use of small cylinders containing radiocobalt, by separating the gold seeds with aluminum spacers (8–10). However, since the gold seeds have almost twice the diameter of the radiocobalt cylinders, tubing with a larger internal diameter is necessary. This larger tubing lacks the flexibility of that used for radiocobalt. In order to overcome this difficulty, a flat, very flexible nylon "ribbon" is being developed in which the seeds are firmly held, without spacers. This ribbon is even more flexible than the nylon tube used for radiocobalt, but occasional breakage due to faulty preparation is still encountered.

Nylon implants are preferred here over needles for removable implants since they provide for (*a*) more accurate implantation, (*b*) better individualization of treatment, (*c*) more comfort to the patient, and (*d*) decreased exposure to the operating personnel.

(*a*) *More accurate implantation* is the first reason for our preference for the nylon technic. As pointed out above, with the present method of permanent implantation, the pattern is not very regular. Stiff needles loaded with radiocobalt or radium can be implanted accurately in parallel rows, but a good pattern is frequently difficult to achieve because of the necessity of "crossing of the ends." This limitation can easily be avoided in nylon applicators by loading the ends with more active sources.

(*b*) *Better individualization* is a second reason for preferring nylon applicators over needles. The nylon tubes are loaded individually for each patient. After use, they are discarded by putting them in a dump until the residual radioactivity subsides. The implantation is usually planned in such a way as to give the desired dose in seven days. During this time, 84 per cent of all the ionizing energy of the radiogold seeds is spent. Only rarely does the pattern deviate from the planned arrangement of sources. Adjustments are made by withdrawing applicators at different times. This is a worthwhile advantage compared with permanent implants, where no adjustment is possible after the implantation.

Various patterns of loading have been used. In most instances, either seeds of equal strength were distributed uniformly throughout the implant, or nylon applicators were loaded more heavily along the edges to give a more uniform dose throughout the treatment area, according to the principles laid down by Paterson and Parker.

(*c*) *Greater comfort to the patient* is a third reason for preferring nylon applicators over stiff needles. This is especially true for curved surfaces and in locations

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where muscular movements normally occur frequently. A nylon implant also stays in place better than a needle implant. Fixation of the ends of the applicators with adhesive tape or clips is usually adequate, and it is not necessary that they be sutured in place.

(*d*) *Decreased exposure to operating personnel:* Since the ends of the nylon applicators are stretched into filaments several feet long, the loaded part can be shielded within a lead carrier, while the unloaded ends are sutured through the tumor. Following this, the radioactive parts of the applicators can be pulled into place in a few minutes. Because the total exposure to personnel is the product of time and dose-rate, keeping the time as short as possible usually reduces the total-body radiation received by the operator, as well as the dose to the hands, to less than the permissible dose.

Two cases may illustrate the accuracy of nylon implants, the individualization of the pattern, and the comfort of the patient during the time the implant is in place.

CASE VI: A white housewife, 42 years of age, gave a history of small multiple skin nodules appearing twenty-five years earlier and increasing slowly in number and size without causing any annoyance. After two years, medical advice was sought and a diagnosis of neurofibromatosis (von Recklinghausen) was made. Some six years later the patient noticed that a small lump in the right supraclavicular area kept enlarging, causing radiating pain. Fifteen years before she was seen in this hospital, a diagnosis of fibrosarcoma originating in a neurofibromatous nodule was made. External radiation therapy (dose and quality unknown) had been given intermittently at monthly intervals during the intervening years, and apparently checked the growth quite effectively.

In May 1953, the patient came to this hospital because the node had begun to grow rapidly and was causing severe pain. Surgical consultation was obtained, and opinion as to the resectability of the tumor was divided. The radiotherapy department was in favor of resection, but the surgical department decided against it. Since it appeared that, by proper selection of fields, the heavily irradiated skin area could be avoided, another course of x-ray irradiation was given, a tumor dose of 4,000 r being delivered from two opposing fields in an overall time of sixty days. This gave good relief of pain, and the tumor was reduced in size by about 50 per cent. Three months later, however, the patient returned with recurrence of pain. It was then decided to try an implant of radiogold seeds in nylon applicators. This was carried out under good sedation and right cervical block. A uniform distribution of the seeds was chosen (Fig. 6) in order to get a higher tumor dose in the center of the mass. The tumor dose in the implanted area was calculated to be 6,000 r on the basis of Quimby's tables. When the patient was last seen, the pain was considerably relieved and the mass had disappeared completely. However, above the original mass and outside the field of implantation, a new mass had developed which was pressing on the brachial plexus. Another implantation into this mass is scheduled.

Fig. 6. Case VI. Nylon implant with radiogold seeds used for treatment of a fibrosarcoma in right supraclavicular region. Uniform loading of the nylon applicators.

CASE VII: An 80-year-old white woman had a Grade I squamous-cell carcinoma of the cheek, resected three times in two years: May 1951, August 1952, and July 1953. She now presented another recurrence in the same area. In view of her age, radical surgery was not advised, and an implantation of radiogold seeds in nylon tubing was carried out on Sept. 29, 1953. The pattern is shown in Figure 7, being curved in such a way as to have a slightly larger spacing in the middle. The seeds on the inside were only about half as strong as the outer ones, even though they were longer, because they were made from an earlier shipment of radiogold wire. Calculations in accordance with the Paterson-Parker tables gave a tumor dose of 6,000 r during the week the implants remained in place. The patient was dismissed from the hospital a day after the implantation was made.

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Fig. 7. Case VII. Nylon implant with radiogold seeds for treatment of a recurrent carcinoma of the cheek. Differential loading with longer but weaker seeds in the middle.

During the week of irradiation, this sensitive, frail old lady felt very comfortable and had no difficulties in eating or speaking. She returned for removal of the implant, which was easily carried out without sedation. A moderate mucositis developed, which cleared up in three weeks. When the patient was last seen, two months after the implantation, she presented no evidence of tumor or radiation reaction. This case also illustrates that patients with implants in nylon tubing can be treated without hospitalization.

Clinically, the same responses in tumors and normal tissues have been observed as were encountered previously with comparable implantations of radiocobalt in nylon tubing (8–10).

SUMMARY

Clinical experience in the first 100 patients treated at the Ohio State Medical Center with radiogold seeds has shown that these seeds can be used successfully as replacements for radon seeds. The simplicity of protection and the ease and rapidity of preparation of radiogold seeds of uniform strength are advantageous. No appreciable differences in therapeutic response were observed as compared with radon seeds.

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SUMARIO

Las Semillas de Radio-Oro en la Radioterapia Clínica

Las observaciones clínicas en los primeros 100 enfermos tratados con semillas de radio-oro en el Centro Médico del Estado de Ohio han demonstrado que pueden usarse con éxito esas semillas como substitutos de las de radón. Usáronse

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cuatro métodos de aplicación: en moldes, en aplicadores intracavitarios, en implantes permanentes y en aplicadores extraíbles de nilón.

La fácil y rápida preparación de los implantes de radio-oro y lo sencilla que es la protección resultan ventajosas. En lo que se ha observado, la respuesta terapéutica no discrepa de la obtenida con las semillas de radón.

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