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Radiogold Seeds for Cancer Therapy

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Many shortcomings of radon seeds for medical use are overcome with the Au^{198} seeds described here. A simple fabrication method has been developed, and refinements have been made in the Nylon-tube implantation technique

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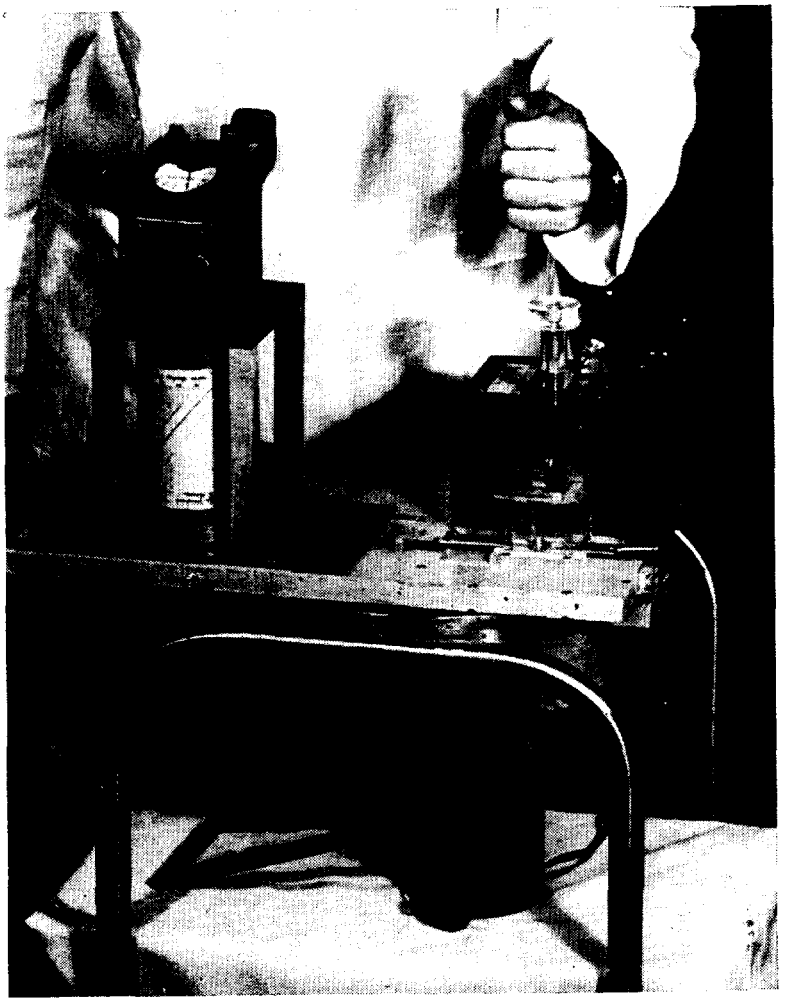

FIG. 1. Encased radiogold wire is extruded from lead shield. Meter at left indicates strength; slight blow on plastic head cuts seed, which falls through tube into shielded container where electric heater sterilizes seed

Radiogold Seeds for Cancer Therapy

RADIOGOLD SEEDS and linear sources developed during the past three years (*1–5*) have displaced radon completely in radiation therapy at The Ohio State University Medical Center. These sources are now used advantageously in many types of cases in which radioactive cobalt was formerly applied (*6–10*).

In external appearance the Au^{198} seeds are indistinguishable from the usual radon seeds, and they can be utilized in the same manner and with the same apparatus. The half-life of Au^{198} is 2.70 days, which is about 0.7 of the half-life of radon (3.83 days). The energy of the gamma radiation emitted by Au^{198} is 411 kv: it is monoenergetic in contrast with the range of energies between 184 kv and 2.198 kv for the dozen different gamma rays emitted by radon and its disintegration products (*11*). Further biological studies (*1, 2*) are under way to determine the relative merits of the differences in half-lives and gamma-ray energies of Au^{198} and radon.

Sources for interstitial applications should not be confused with radioactive gold in the colloidal state which is now being used in some medical centers for the treatment of pleural and peritoneal carcinomatosis. In contrast to colloidal Au^{198}, in which the beta radiation emitted by the radiogold is used primarily, gold seeds containing Au^{198} are employed only because of the

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gamma rays emitted from the radiogold within them. The seeds are usually superior because of the relatively homogeneous dosage of ionizing radiation that may be achieved when discrete sources of gamma rays are properly spaced in accordance with well-established physical principles. Dosimetry is highly uncertain whenever radioactive sources are injected that are mainly dependent on the emission of beta particles for whatever effectiveness they may have. The Au^{198} seeds are, therefore, essentially similar to radon seeds, where much of the beta radiation is removed by filtration.

Advantages of Au^{198} seeds over radon seeds for applications in therapy include:

1. Radiogold seeds of any strength can be cut instantly, even at the time the decision to use them is made (e.g. in the operating room), whereas radon seeds usually must be ordered a day or more in advance of the time they are to be used.

2. Radiogold seeds are very uniform in strength, but wide variations in strengths are often found in radon seeds.

3. Because gold is a metal there is no danger of leakage of gas from Au^{198} seeds.

4. The beta particles emitted by Au^{198} with maximum energy of 970 kv are almost completely filtered out, in contrast to the beta particles emitted by radon disintegration products with maximum energy of 3,170 kv.

5. The facilities and equipment required for manufacturing seeds loaded with Au^{198} are simple and inexpensive.

6. Problems of protection are greatly simplified in the preparation and handling of Au^{198} seeds because the half-value layer in lead for the gamma rays is only 2.8 mm, in contrast to 14 mm for radon.

Preparation of Sources

Each Monday there arrives in Columbus via air express a package shipped by the Oak Ridge National Laboratory earlier that day. This package contains several pure gold wires† 0.2–0.3 mm in diameter and 85 mm long that have been irradiated during the previous week in a flux of about $1\text{–}5 \times 10^{11}$ thermal neutrons/cm^2/sec in a nuclear reactor. In the radioisotope laboratory the radioactive wires are slid into inert gold tubing† about 0.4 mm inside and 0.8 mm outside diameter. This nonradioactive outer gold tubing absorbs almost all of the beta particles and passes about 90% of the 411-kv gamma rays emitted by the radioactive gold wire contained within it.

Seeds are cut to any desired strengths with a simple cutter. The device consists of a lead block with a central bore into which the encased radioactive gold wire is introduced and from which it may be extruded to any desired length from 1 to 40 mm, preadjusted by a micrometer. The gamma radiation of the part of the encased radioactive gold wire pushed outside of the lead shield to be cut off with the cutter, is measured with a radiation survey meter equipped with an ionization chamber ("Cutie-Pie" type).

FIG. 2. Six Nylon tubes were used to implant radiogold seeds in residual tumor at base of tongue after radical surgery. Dummy seeds used first, then replaced with active seeds to give minimum tumor dose of 5,200 r in 7 days

Calibration of seed strength. The survey meter is placed in a fixed position at such a distance from the cutter that a swing of the needle to 20 scale divisions on the 50 mr/hr full-scale range of the meter will result in a Au^{198} seed which will deliver 1,000 gamma roentgens-total-at-one-centimeter (designated "rtcm") during complete decay. This is approximately the same strength as the 1,112 r given off during lifetime decay of 1 mc of radon enclosed in 0.5 mm. of platinum. The cutter is portable and is often taken to the operating room where Au^{198} seeds are calibrated and cut in a few seconds. (See Fig. 1.)

Details of design of the cutter, of the method of calibration of the sources, and of dosimetry with the Au^{198} seeds will be published separately.

Following publication (*1*, *2*) of the method developed here for making sources containing Au^{198}, Sinclair (*12*) briefly described sources made from cylinders of gold sealed in a platinum beta-particle absorber before exposure to the neutron flux in a nuclear reactor. The method described here for preparing Au^{198} seeds would appear to be a superior one in the following respects:

1. The radiation therapist has all of the advantages of on-the-spot adjustability of strengths of sources provided by a radon plant without the many well-known disadvantages associated with the establishment and operation of a radon plant. The method described by Sinclair does not permit adjustment of strengths of sources at the point of usage, nor does it enable the therapist to compensate for decay of radioactivity by making longer seeds or by using successively thicker radioactive gold wires irradiated in the same container in the nuclear reactor, during the latter part of the week they are received.

Radiogold seeds received from a distant point of preparation will always put the therapist to the same disadvantages that now prevail for those physicians who receive radon seeds from commercial sources. The variation of source strengths to provide the flexibility required for individualization of patterns to meet the multitudinous clinical variations encountered in practice, is not possible with sources of initially fixed strengths.

2. It was shown previously (*3*, *5*) that the leakage of the undesirable beta particles through the thinned parts of the ends of Au^{198} seeds prepared here is insignificant in comparison with the escape of highly energetic and penetrating beta particles from a radon seed obtained from a commercial source. Measurements made by Sinclair revealed a beta-particle emission from the platinum-sheathed Au^{198} sources he prepared that differed only slightly from that of radon seeds.

3. The cost of nonradioactive gold for sheathing material to absorb the

† Supplied by the American Platinum Works, Newark, New Jersey.

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same fraction of the beta particles emitted from the enclosed radiogold is only about one-fourth as great as that for the platinum sheaths used by Sinclair. Moreover, the expense incurred for the precision machining and welding that is required to encapsulate the gold within the platinum is avoided in the method devised here.

Clinical Uses

Radiogold seeds may be utilized to form permanent implantations by means of the same applicators that are now widely used for radon seeds. Alternatively, Au^{198} seeds may be loaded into Nylon tubing that is threaded through tumors and withdrawn at the end of the exposure time, which is usually 7 days. An advantage of implanting Au^{198} seeds permanently is that it is unnecessary to load the seeds into Nylon tubing. However, permanent implantations by free-hand techniques have not resulted in the regular patterns of sources that are usually obtained readily when the seeds are first enclosed in Nylon tubing.

Another advantage of the Nylon-tube method is that errors in alignment of the pattern during implantation can be corrected by pulling the Nylon tubes into the proper position, as indicated by roentgenograms. Also, no foreign body remains in the tissue after the Nylon tubes are withdrawn at the end of a week. Experiences at this medical center have demonstrated that the Nylon-tube technique is generally to be preferred to the permanent implantation of the seeds.

Improved implantation method. The Nylon-tube implantation method, previously developed here for use with Co^{60} (*8–10*), has recently been improved in several respects. Since details of this new Nylon-tube technique will be reported independently by Henschke, only the principal features of it will be outlined briefly here. First, in place of the thick-walled, relatively stiff Nylon tube formerly employed at The Ohio State University Medical Center, a thin-walled, narrow Nylon tube is now used. In this new Nylon tube, the radioactive sources are held firmly in place by the resiliency of the Nylon without the need for the metallic spacers used formerly. These new tubes are much more flexible and can be bent more readily than the previous tubes. Moreover, should the loaded suture break inadvertently, the radioactive sources cannot fall out as they could with the old method.

A second major improvement in the Nylon-tube technique has been evolved and is now used in many cases. The Nylon tubes are not loaded with the radioactive sources prior to implantation; instead, Nylon tubes loaded with dummy metal seeds, or thin stainless-steel wires are inserted in the tumor area at the time of operation. Roentgenograms are then made and an appropriate distribution for the radioactive sources is determined from the spatial relationships. Nylon tubes are loaded with the radioactive sources accordingly and are pulled into position after attachment to the dummy-loaded Nylon tubes or to the stainless-steel wires. This substitution of the Nylon tubes loaded with active sources for the ones containing the dummy sources, or the wires, causes little discomfort and is usually done satisfactorily without anesthesia. (See Fig. 2.)

It will be apparent that this technique enables the surgeon to prepare a patient during operation for subsequent implantation with the radioactive seeds. The radiation therapist can then design an appropriate pattern and insert it at a time and place convenient for him. This technique has proved mutually satisfactory to the surgeon and the radiotherapist members of the team here.

Clinical experience. Fifty-one applications of Au^{198} seeds clinically in 46 patients thus far have included 31 permanent implantations, 12 Nylon-tube implantations, 2 intrauterine applications, 2 intraesophageal applications, 2 nasopharyngeal applications, 1 intraoral mold, and 1 skin mold.

No untoward or unusual reactions have been noted in any case in which the Au^{198} seeds have been used. The clinical regressions of tumor tissue have been comparable to those observed with other methods of interstitial irradiation. And they have been consistent with the preliminary animal experiments in which it was demonstrated that it is possible to deliver a cancerocidal dose to tumor tissue with Au^{198} seeds alone (*1, 2*). However, the preferred practice here usually is to use Au^{198} seeds in combination with high-voltage external irradiation. In some cases two insertions of radiogold seeds spaced 1–8 weeks apart have been used to deliver the total dose over a longer period.

Summary

1. Radiogold seeds are convenient replacements for radon seeds. And they may also be used advantageously in the newer methods of application such as the Nylon-tube implantations.

2. Radiogold seeds are prepared by activating a fine gold wire in a nuclear reactor and then encasing it in an inert outer gold tube in order to filter out the beta particles. The Au^{198} seeds are cut with a special cutter to any desired strengths registered on a radiation meter as the encased radioactive gold wire is extruded from a lead storage shield. The meter is calibrated to give the number of gamma roentgens-total-at-one-centimeter, rtcm, which the seed to be cut will emit during complete decay.

3. The reactions observed clinically in 51 applications in the first 46 patients in which the Au^{198} seeds were used appeared to be similar essentially to those obtained with implantations of radon, radium, or Co^{60}.

* * *

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