A Shielded, Automated Injector for Energetic Beta-Emitting Radionuclides

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Objective: Systemic radiation therapy may require the clinical use of relatively high levels (tens of millicuries) of energetic pure, beta-emitting radionuclides such as ^{32}P, ^{89}Sr and ^{90}Y. To deliver such amounts of radioactivity to the patient presents a unique radiation hazard to the staff in nuclear pharmacy, radiation oncology and nuclear medicine due to the brake, or bremsstrahlung, radiation produced in the injection volume and syringe.

Methods: We designed a portable shield and automated delivery system which can be operated remotely to perform intravenous or intraperitoneal administration of a given amount of radioactivity and in a fixed period of time.

Results: By encasing a 60-cc syringe in 1.4 cm of acrylic and covering that layer with 6 mm of lead, we could reduce the exposure rate to approximately 0.12 mR hr^{-1} mCi^{-1} at 5 cm from the side of the device containing a ^{90}Y source. Corresponding exposure rates were 0.027 and 0.001 mR hr^{-1} mCi^{-1}, at 20 and 100 cm respectively, from the side of the injection syringe. For a 50-mCi clinical injection, we estimated exposure rates of approximately 6 mR hr^{-1} at 5 cm from a ^{90}Y source enclosed in this prefabricated, portable syringe holder.

Conclusions: We recommend that clinics, using high-energy beta emitters for radiotherapy, fabricate acrylic and lead holders for syringes used in the protocols to reduce their staffs' exposure.

Key Words: automated injector; beta-emitting radionuclides; bremsstrahlung radiation; brake radiation

With the development of polyclonal (*1*) and monoclonal (*2*) antibodies, a treatment strategy involving radiolabeled antibodies has been developed for malignant diseases such as lymphoma (*3*), ovarian cancer (*4*), melanoma (*5*) and gastrointestinal cancers (*6*). This strategy uses the venous, lymphatic or intraperitoneal fluids to permit access and eventually to target specifically the relevant malignant tissues and even isolate malignant cells throughout the body of the patient.

Historically, this therapeutic targeting has a precedent in the treatment of thyroid carcinoma with radioiodine (i.e., ^{131}I in the form of sodium iodide (*7*)). In that case, the majority (over 90%) of the radiation dose to the malignant thyroid tissue was beta radiation. Gamma radiation found in the ^{131}I decay scheme, however, has remained a health hazard to clinical staffs and required patient hospitalization until total body burden was under 30 mCi or produced a radiation field level under 5 mrem per hr at 1 m (*8*). Because of these negative safety and hospital cost factors, antibody therapeutic agents have often been designed to incorporate pure beta emitters. Due to poor vasculature and antigen heterogeneity on the tumor surface, high-energy beta emitters such as ^{90}Y have been preferred clinically to allow tumor radiation dose across the neoplasm volume (*9*).

Other systemic therapies, not specific and sometimes only palliative, previously have been prescribed using high-energy beta emitters. These applications include ^{32}P for malignant ascites, ovarian cancer (*10*) and polycythemia vera (*11*). Similarly, ^{89}Sr (*12*) and ^{90}Y (*13*) have been injected for metastatic bone lesions. Yttrium-90 has also been applied via arterial injection into the liver to treat localized metastatic disease (*14*). The shielding strategy described here is directly applicable to these situations as well as to those using radiolabeled antibodies.

The greater use of beta-emitting radiopharmaceuticals has brought about increasing concerns associated with personnel radiation exposure during handling and use. For a tumor to receive an adequate therapeutic dose (i.e., on the order of 5000 rads) the clinician may need to inject tens of millicuries of certain beta-emitting radionuclides (*10–15*). Because of the relatively high energy of the beta emissions, there is a risk of brake radiation dose to personnel involved in the radiation therapy protocol. The probability of brake dose is proportional to both the average atomic number of the stopping material (Z) and the average energy (E_{av}) of the emitted

TABLE 1
Pure Beta-Emitting Radionuclides Used in Systemic Radiation Therapy

Radionuclide	E_{av} MeV	E_{max} MeV	Range (cm) in soft tissue	Relative probability of brake radiation
^{32}P	0.69	1.70	0.80	0.74
^{89}Sr	0.58	1.49	0.70	0.62
^{90}Y	0.93	2.29	1.10	1.00

beta particle (16). Included in Table 1 are the relative probabilities in soft tissue of brake radiation production for the radionuclides considered above.

An automated, shielded delivery system can largely eliminate the problem of brake radiation exposure. Staff would not be required to push the injection syringe plunger and, therefore, not be in continuous close proximity to the source of bremsstrahlung x-rays. Additionally, brake radiation exposure at large distances could be reduced via shielding of sequential layers of acrylic and lead.

MATERIALS AND METHODS

A standard commercial pump was modified, as shown in Figure 1, with a large aluminum plate 11.3 cm wide by 5.0 cm high and 2.5 cm thick which enabled a uniform pressure to be exerted on the syringe plunger. An analogue meter was added to the monitor panel so fluid pressure could be monitored remotely. This permitted the technologist or physician to inject from a distance to reduce radiation exposure. A secondary benefit of this technique was the ability to produce a fixed rate of infusion while staff monitored the patient for drug reaction symptoms.

An acrylic cover was designed to go on the outside of a specific 60-cc syringe (wall thickness approximately 1 mm). The syringe holder was a hollow cylinder of 1.4-cm acrylic inside and a 6-mm lead outer layer. This cover, which had removable end plates, was placed over the syringe immediately after the dose was assayed to minimize exposure to the radiopharmacy staff. The outside diameter of the device was 7.0 cm with a total length of 17.9 cm.
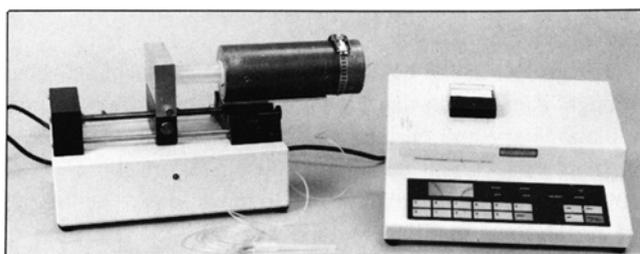
An important consideration is that not all manufacturers produce syringes with the same outside diameter. In this device, the shield was made for a particular 60-cc syringe. Attempts to insert other manufacturers' syringes into the shield may be impossible or cause a radiation-leaking gap between the plastic syringe and the acrylic shield.

The order of the shielding materials was important as the acrylic acted initially to stop all electrons coming from the source (Table 1). Subsequent brake x-rays arising from the stopping process were then attenuated by the outer layer of lead. A cap of the same layers of plastic (1.9 cm) and lead (6 mm) was placed on the end of the cylinder nearest the patient to reduce edge exposure in that direction. A set of long plastic inserts was included at the injection end to prevent electrons from emerging along the plunger. These features are demonstrated in Figure 2. A small cart was used to transport the syringe holder to the clinic.

In the radioimmunotherapy treatment room, the holder was removed from the cart and inserted directly into the modified pump apparatus (Fig. 1). Individual patient parameters were entered into the remote control and the infusion was begun after the patient passed a challenge test using a small amount (e.g., 0.1 mg) of the antibody about to be injected.

Radiation exposure rates around the syringe holder and pump apparatus were measured using a ^{60}Co-calibrated, hand-held Geiger-Mueller counter. This calibration point was significant in that we have previously shown that the half-value layer for brake radiation emerging from several centimeters of tissue-equivalent material is similar to that found for ^{60}Co (17). For these measurements, various sources of ^{90}Y were contained in 60 cc of saline in the syringe. Such a volume is appropriate for the injection of a 5-mg dose of cT84.66, a chimeric anti-CEA monoclonal antibody developed to target colorectal tumors (18). These measurements were repeated two times. In addition, a single measurement was taken at 1.5 m from the side of the syringe without the shield in place so as to estimate the intrinsic exposure rate.

RESULTS

Radiation exposure rates were evaluated both along and perpendicular to the long axis of the syringe holder. Average

FIGURE 1. Automated, modified pump apparatus and mounted syringe shield. Note the large aluminum block inserted onto the driving screw in order to exert uniform pressure on the plunger shaft. The control chassis is shown on the right. An analogue meter has been added to the top of the chassis to indicate fluid pressure.
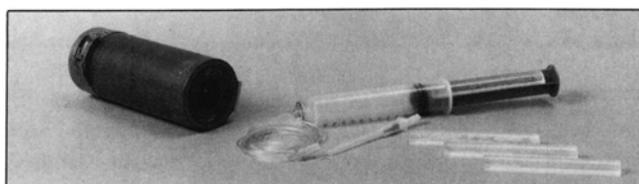
FIGURE 2. Portable, high-energy beta shield with 60-cc syringe removed at right. Acrylic thickness was set at 1.4 cm, which is appropriate for ^{90}Y. Six mm of lead have been placed outside the acrylic to reduce the brake radiation exposure. Quarter-round acrylic inserts are shown partially removed; these are placed along the plunger shaft to reduce beta exposure in a direction retrograde to the injection.

TABLE 2
Exposure Rates at Various Positions Around the Shielded Syringe Holder Enclosing a Yttrium-90 Source

Distance In cm	Normalized rate of exposure in mR hr^{-1} mCi^{-1}
a) Perpendicular to centerline of shield	
Surface	0.300
5.0	0.120
20.0	0.027
100.0	0.001
b) Toward patient (along centerline of shield)	
Surface	0.110
5.0	0.056
20.0	0.011

results for the two measurements are given in Table 2. It was found that the highest rates, 0.12 mR hr^{-1} mCi^{-1}, were found alongside the holder at 5 cm from its center line. At 20 cm from the center line, the average exposure value was 0.027 mR hr^{-1} mCi^{-1}. A rate of 0.056 mR hr^{-1} mCi^{-1} was obtained 5 cm from the end of the housing toward the patient. At distances of one meter or more from the midline, exposure rates were essentially at background levels (0.015 mR/hr) for a 10-mCi source of ^{90}Y.

The bare syringe exposure rate at 1.5 m was 0.65 mR hr^{-1} mCi^{-1}. Using an inverse-square correction to 5 cm, the expected value was 585 mR hr^{-1} mCi^{-1}. Because of safety considerations, we did not measure the radiation field at this short distance. It would appear, however, that the protection afforded by the shielding was approximately four orders of magnitude (i.e., 0.12/585 or 2.0 × 10^{-4}).

Most of the protection is due to the stopping of high-energy betas from ^{90}Y. From our earlier measurements from a point source of ^{90}Y (17) in tissue-equivalent material, we would estimate a brake radiation exposure rate of 1.7 mR hr^{-1} mCi^{-1} at 5 cm from the side of the acrylic-covered syringe. This is only 2.9 × 10^{-3} of the total radiation field estimated at 5 cm. Yet even this magnitude is over ten times larger than the measured value of 0.12 mR hr^{-1} mCi^{-1}. Thus, adding the layer of lead has reduced exposure by approximately an additional factor of ten by attenuating brake radiation.

DISCUSSION

It is important to realize that x-ray exposure of personnel is possible while injecting a pure beta emitter. Moreover, brake radiation produced during the stopping of high-energy betas can be highly penetrating. For example, the radiation emitted from a patient containing ^{90}Y would have a half-value layer comparable to that of ^{60}Co (17). Thus, we may anticipate a measurable radiation dose to clinical staff during an injection of tens of millicuries of this radionuclide. It is

important to design a shielded, transportable container to allow safe movement of a loaded syringe from the radiopharmacy to the clinical site.

A syringe holder fashioned of 1.4 cm acrylic and 6 mm lead can reduce the personnel exposure rates to background values at distances of approximately one meter from the long axis of the syringe holder containing ten mCi of ^{90}Y. This holder can be loaded in the nuclear pharmacy to reduce exposure of personnel both there and during transportation to the clinical area. At near distances, such as 5 cm from the shielded syringe, the reduction in brake radiation exposure rate was approximately ten-fold due to the lead layer.

We recommend that clinics performing radiotherapy using high-energy beta emitters, such as ^{32}P, ^{89}Sr or ^{90}Y, fabricate acrylic and lead holders for the variously sized syringes used in the protocols. Using shielding and a remote injector can significantly reduce the exposure of nuclear pharmacy and clinical personnel.

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