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Technical note

InfuShield: a shielded enclosure for administering therapeutic radioisotope treatments using standard syringe pumps

Dominic P. Rushforth^a, Brenda E. Pratt^a, Sarah J. Chittenden^a, Iain S. Murray^a, Louise Causer^b, Matthew J. Gray^a, Jonathan I. Gear^a, Yong Du^b and Glenn D. Flux^a

The administration of radionuclide therapies presents significant radiation protection challenges. The aim of this work was to develop a delivery system for intravenous radioisotope therapies to substantially moderate radiation exposures to staff and operators. A novel device (InfuShield) was designed and tested before being used clinically. The device consists of a shielded enclosure which contains the therapeutic activity and, through the hydraulic action of back-to-back syringes, allows the activity to be administered using a syringe pump external to the enclosure. This enables full access to the pump controls while simultaneously reducing dose to the operator. The system is suitable for use with all commercially available syringe pumps and does not require specific consumables, maximising both the flexibility and economy of the system. Dose rate measurements showed that at key stages in an ¹³¹I mIBG treatment procedure, InfuShield can reduce dose to operators by several orders of magnitude. Tests using typical syringes and infusion speeds show no significant

alteration in administered flow rates (maximum of 1.2%). The InfuShield system provides a simple, safe and low cost method of radioisotope administration. *Nucl Med Commun* 38:266–272 Copyright © 2017 The Author(s). Published by Wolters Kluwer Health, Inc.

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^aJoint Department of Physics, The Royal Marsden NHS Foundation Trust and ^bDepartment of Nuclear Medicine, The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey, UK

Correspondence to Dominic P. Rushforth, MPhys, Joint Department of Physics, The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey SM2 5PT, UK

Tel: +44 208 642 6011 ext. 1397; fax: +44 208 643 3812; e-mail: dominic.rushforth@rmh.nhs.uk

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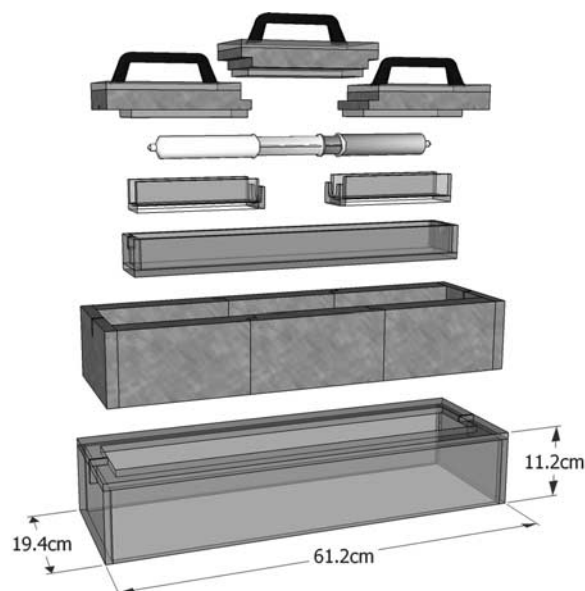
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Introduction

¹³¹I mIBG and ⁹⁰Y/¹⁷⁷Lu DOTATATE are routinely administered for radioisotope therapy [1]. The administration of such therapies presents a number of challenges: the infusion must be given at a steady gradual rate to minimize potential complications [2]. The operator should be able to monitor and alter the rate of flow as the infusion takes place. It must also be possible to stop the infusion quickly and easily in the case of an emergency. The equipment should contain spills and leaks to minimize the risk of radioactive contamination. It must also be easy to clean to satisfy infection control requirements and facilitate decontamination. The equipment should also appear professional, represent good value for money and, ideally, be easy to store and transport. Of particular importance, the absorbed dose to staff and the public must be as low as reasonably practicable [3]. This technical note details a system designed to administer such therapies while fulfilling all of these criteria.

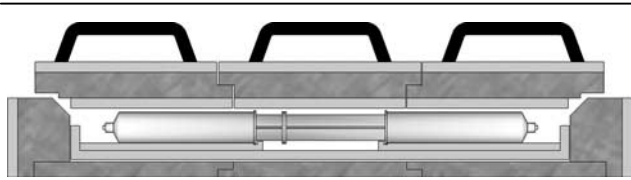
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Fig. 1



The components comprising InfuShield. From top to bottom; lids (x3), internal syringes (x2), inserts (x2), liner, lead shielding, outer cover.

Fig. 2



Cross section of InfuShield showing the intravenous line labyrinths.

Materials and methods

Construction

Designed and constructed entirely in house, the InfuShield device was created to safely contain therapeutic quantities of ¹³¹I, ⁹⁰Y and ¹⁷⁷Lu. The device consists of multiple components (Fig. 1) that, when assembled, surround two back-to-back syringes with three encasing layers (Fig. 2); a core of Perspex (light grey), a layer of lead shielding (dark grey) and an outer shell of Perspex.

At the centre of the device, a liner box holds interchangeable inserts into which syringes slot easily and quickly. Inserts were created to hold 30 and 50 ml syringes; inserts for other syringe sizes could be easily fabricated. The liner is watertight and easy to decontaminate in case of spills. Constructed of Perspex, the liner and inserts also attenuate the high energy electron emissions of isotopes such as ⁹⁰Y (principal β emission: 2279 keV [4]).

The lead shielding (Table 1) was designed to attenuate the γ emissions from therapeutic quantities of ¹³¹I (principal γ emission: 364 keV [5]) to acceptable levels. This ensured that it would also be sufficient for ¹⁷⁷Lu (principal γ emission: 112 keV [6]) and any Bremsstrahlung produced in the Perspex. The individual sections of lead shielding interleave so that there are no direct beam paths through the shielding. Narrow labyrinths for the intravenous lines (Fig. 2) also minimize radiation leakage, while being straight enough to allow the easy and rapid insertion of syringes containing therapeutic levels of activity.

The Perspex outer shell covers, protects and holds in place the interlocking lead bricks. This gives the device a robust exterior that can be easily cleaned; satisfying both decontamination and infection control requirements.

The lids were also constructed of three layers, consisting of lead sandwiched between sheets of Perspex. This

combination provides shielding for β and γ radiations, protects the soft lead from knocks and facilitates cleaning. The lids interleave with one another, requiring the middle lid to be inserted last and removed first, to ensure there are no gaps in the shielding. Strong and ergonomic nylon handles provide secure grips for manipulating the lids, which weigh 6 kg. This is in line with the Health and Safety Executives general guidance [7], which recommends a maximum load of 7 kg for items that are lifted between mid-lower leg and shoulder height.

In total InfuShield weighs 98.6 kg. Even accounting for a robust trolley to support it, this is well within the guideline levels for pushing and pulling over a flat, level surface using a well-maintained handling aid [7]. In addition, its low centre of gravity makes the device inherently stable during transport.

Function

In all, the device requires three identical syringes. The syringe containing radioactivity (labelled C in Fig. 3) is driven by a second syringe (B in Fig. 3) which is filled hydraulically, via a flexible intravenous line, by a third syringe (A in Fig. 3) that is in turn driven by a syringe pump. In our centre Alaris GH syringe pumps (Alaris; Cardinal Health, Rolle, Switzerland) are used, although any syringe pump could be accommodated.

Following administration, saline is used to flush out any remaining activity from the therapy syringe and intravenous line. This ensures the full administration of the prescribed activity and minimizes residual contamination. The syringe driver is disengaged from the plunger of syringe A and a three-way tap turned so that the contents of the saline syringe (D in Fig. 3) can be pushed into syringe C (simultaneously reversing syringes A and B). The three-way tap is then returned to its original position, the syringe driver is re-engaged with syringe A and the pump is used to drive the flush into the patient.

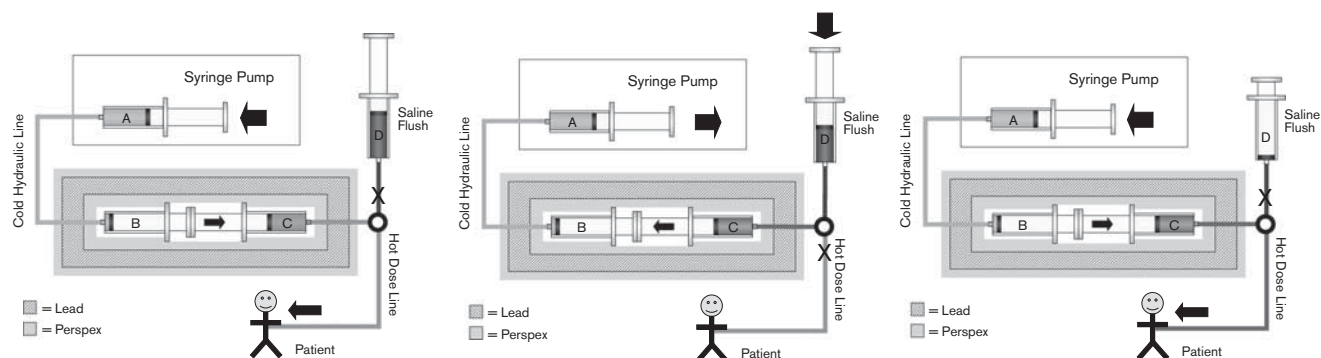
Syringes A and B and the line connecting them form a sealed hydraulic system. The system is prepared in advance of and separately from the therapeutic administration. Saline is used as the hydraulic fluid; this is coloured with food dye to ensure that the hydraulic components are instantly distinguishable from patient lines. The syringes are also labelled and syringe A is marked to show the fluid volume that remains when syringe C is emptied.

Interchangeable inserts permit the use of a variety of syringe sizes and types. It is essential that syringes A and B have the same internal cross section so that syringe C is driven at the speed set by the pump. As the Alaris pump automatically detects the inserted syringe type and uses this to determine the plunger speed required, syringe A (and therefore B) must also be identical to syringe C to ensure that the correct rate is selected. To ensure

Table 1 Thickness of lead shielding in InfuShield and resulting γ attenuation

| | Thickness of lead (cm) | Theoretical ¹³¹ I attenuation | Theoretical ¹⁷⁷ Lu attenuation |
|-------|------------------------|------------------------------------------|-------------------------------------------|
| Base | 1.5 | 1/30 | 1.33 × 10 ⁻⁷ |
| Top | 2.5 | 1/118 | 3.43 × 10 ⁻¹² |
| Sides | 5 | 1/2560 | 1.05 × 10 ⁻²³ |

Fig. 3



InfuShield in use.

Fig. 4

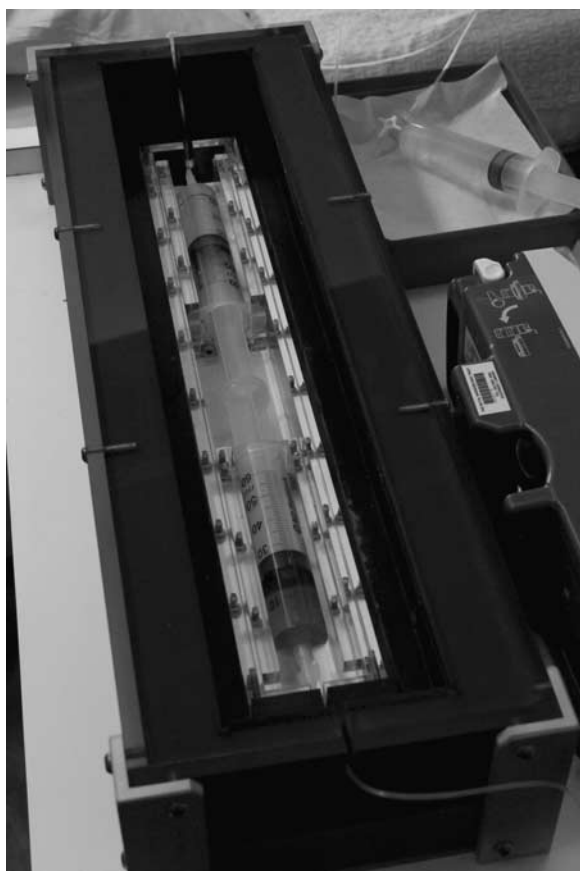


Photo of InfuShield, with lids removed, set up for an infusion using a 50 ml syringe.

compliance every insert carries a warning, stating ‘All three syringes must be of the same size and type’.

Figure 4 shows the completed device as set up when performing an infusion. The lids would normally be in place during an infusion but were removed so that the

internal workings could be shown. The rear of the Alaris pump driving InfuShield can be seen on the right of the image.

Testing methodology

Before clinical use, tests were carried out to investigate the effect of the device on administered flow rates and the functioning of the occlusion alarm.

Flow rate

The InfuShield system was set up as described in the ‘Function’ section, using BD plastipak syringes (Becton Dickinson, Franklin Lakes, New Jersey, USA), a BD Connecta three-way tap, an Alaris GH syringe pump and 50 cm lines of 1 mm internal diameter. At the end of the administration line, in place of the patient in Fig. 3, a 22 G Braun winged safety intravenous catheter (Braun, Melsungen, Germany) was attached to a clamp above a beaker resting upon a calibrated Sartorius 1474 MP 8-2 electronic scale (Sartorius, Goettingen, Germany). The InfuShield device was then used to drive a syringe of water, which dripped from the catheter into the beaker. A webcam was used to record the weight of the beaker at 60 s intervals, until the administration syringe had been emptied and the pump stopped.

The test was carried out with both 30 and 50 ml syringes, using three different infusion speeds (30, 60 and 90 ml/h) that cover the range normally used for clinical administrations. For comparison each test was repeated without using InfuShield, with the syringe pump driving the administration syringe directly.

F-tests were carried out on the acquired measurement data using the Excel data analysis (two sample for variances) package, to determine if there were any statistically significant differences in the variances of the results when InfuShield was used.

Occlusion alarm

The Alaris GH syringe pump, in common with other pumps, has an occlusion alarm that is triggered when the pressure exerted by the pump exceeds a set limit. The purpose of the alarm is to warn the user that the line is blocked and to stop an excess of pressure building up in the line. Once an occlusion occurs it takes time for the pressure to reach the level required to trigger the alarm. A test was devised to determine what effect InfuShield would have on the alarm.

Using the same apparatus as used to test flow rate, the pump was set to a rate of 90 ml/h and allowed to run until a continuous flow was passing through the entire apparatus. The three-way tap was then closed and a stopwatch timer simultaneously started. The timer was halted as soon as the occlusion alarm sounded. The measurement was repeated 30 times, both with and without the InfuShield device in place.

Shielding

Dose rate measurements were acquired to confirm that the shielding functioned as designed. A 5.8 GBq NaI capsule was placed in the position of the active syringe and measurements were taken from a variety of positions at a distance of 50 cm; this being the approximate distance between the shielding and the torso of an individual pushing the trolley. For comparison dose rate measurements were also made of the capsule when unshielded and when contained within a typical syringe box. Results were adjusted to give dose rates for a typical administered activity of 7.4 GBq (assuming a normal activity range of 3.7–11.2 GBq [2]). The same methodology was used to make dose rate measurements with therapeutic ⁹⁰Y administration syringes in place within the system.

Staff doses

To determine the staff doses received during administrations, the Clinical Nurse Specialist (CNS) performing the procedure routinely wore an Electronic Personal Dosimeter during the treatments.

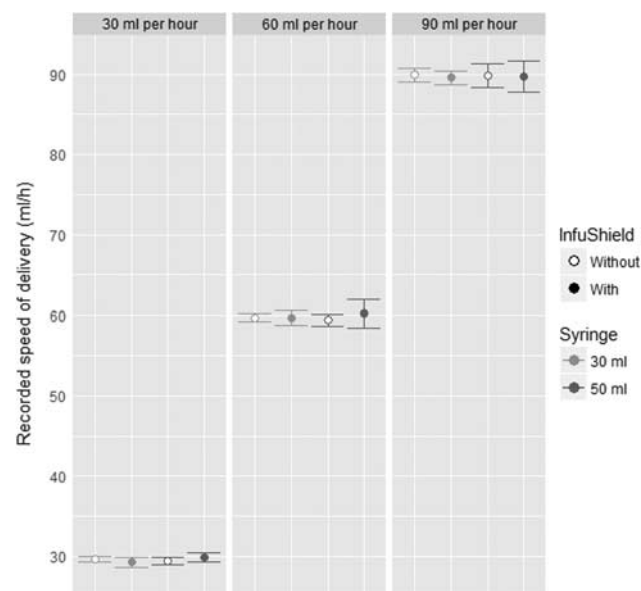
Results

Flow rate

Figure 5 shows the average flow rates recorded for each of the set ups, along with the SDs of the results. Table 2 shows the same results along with the results of the statistical analysis.

Measured flows showed a high level of consistency with the set flow rates, both when the syringes were directly driven by the pumps and when driven using InfuShield. The largest measured average difference in flow rate resulting from the addition of the InfuShield device was 1.21%.

Fig. 5



Flow rates recorded with the syringe directly driven by the pump and by InfuShield using 30 and 50 ml syringes. Readings were performed with the pump set to 30, 60 and 90 ml/h. Error bars show the SD of measurements taken at 1 min intervals.

For all combinations of syringe size and pump speed, the variance in readings increased when InfuShield was used. The results of the *F*-tests show that these increases are statistically significant for those readings carried out at 30 and 60 ml/h. The largest increase in variance was for 50 ml syringes being driven at 60 ml/h, where the coefficient of variation was more than double, from 1.31 to 2.99%.

Occlusion alarm

Figure 6 shows the results of the occlusion alarm test. On average the use of InfuShield increases the time to alarm from 14.6 to 22.3 s.

Shielding

The dose rate measurements carried out with ¹³¹I are shown in Table 3. Maximum dose rates 50 cm from InfuShield (horizontally) are 1081 times less than for an unshielded source of the same activity and 293 times less than for the same activity contained within a syringe box. Dose rate measurements (and even count rate measurements using mini Geiger monitors) with ⁹⁰Y were too low to be distinguished from background.

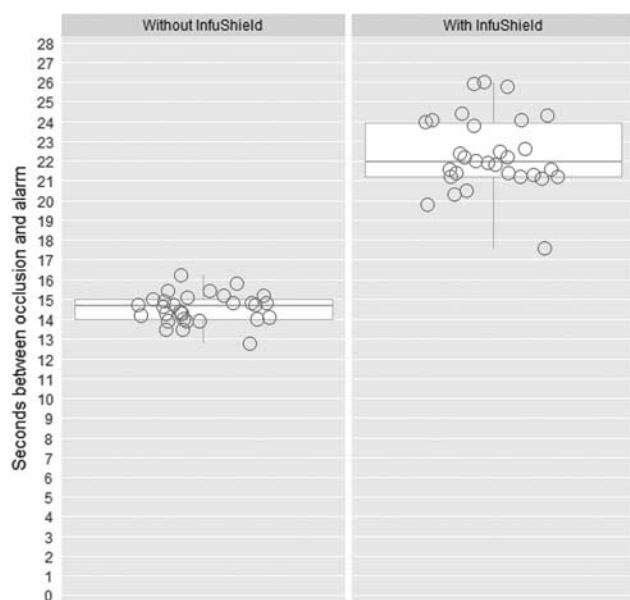
Staff doses

Nine Electronic Personal Dosimeter staff doses were recorded for the CNS during the administration of ¹³¹I mIBG treatments (activity range: 4.5–22.3 GBq) using InfuShield. These showed a mean ± SD dose of 58.8 ± 43 µSv per treatment with a range of 18–141 µSv. There was no significant correlation between the activities administered and the doses

Table 2 Results from flow rate measurements

| Infusion speed (ml/h) | 30 | | | | 60 | | | | 90 | | | |
|------------------------------|----------|-------|----------|-------|----------|-------|----------|-------|---------|-------|---------|-------|
| Syringe size (ml) | 30 | | 50 | | 30 | | 50 | | 30 | | 50 | |
| Infushield in line | Without | With | Without | With | Without | With | Without | With | Without | With | Without | With |
| Number of readings | 58 | 51 | 112 | 91 | 30 | 24 | 55 | 48 | 20 | 15 | 38 | 33 |
| Mean speed (ml/h) | 29.62 | 29.26 | 29.47 | 29.85 | 59.72 | 59.72 | 59.40 | 60.21 | 89.92 | 89.58 | 89.84 | 89.70 |
| Difference in speed (%) | -1.23 | | 1.29 | | 0.01 | | 1.36 | | -0.38 | | -0.16 | |
| Coefficient of variation (%) | 1.18 | 2.23 | 1.54 | 1.94 | 0.87 | 1.51 | 1.31 | 2.99 | 0.99 | 0.95 | 1.67 | 2.19 |
| Difference in CoV (%) | 89.38 | | 26.11 | | 73.19 | | 129.19 | | -4.28 | | 31.48 | |
| $F > F_{\text{Critical}}$ | True | | True | | True | | True | | False | | False | |
| P value | 3.81E-06 | | 7.13E-03 | | 2.88E-03 | | 4.55E-09 | | NA | | NA | |

NA, Not applicable.

Fig. 6

Dotplots of time taken to trigger the alarm after an occlusion, with and without InfuShield, superimposed over box plots of the same data.

Table 3 Dose rates from 74 GBq of ^{131}I

| Positions | Doses ($\mu\text{Sv/h}$) |
|------------------------------------|----------------------------|
| 50 cm from end containing activity | 1.1 |
| 50 cm from end opposite activity | 0.6 |
| 50 cm from the sides | 1.6 |
| 50 cm above the top | 13.9 |
| 50 cm below the bottom | 38 |
| 50 cm from source in syringe box | 469 |
| 50 cm from unshielded source | 1730 |

received by the CNS, $r=0.46$, $P=0.21$. Mean dose per unit absorbed activity was $6.7 \pm 6.2 \mu\text{Sv/GBq}$.

Discussion

The number and range of radionuclide therapies continue to expand with the clinical introduction of new radiotherapeutics. There is also increasing evidence that because of the range of absorbed doses delivered from

fixed activities, personalisation of treatment may entail the administration of higher activities than have previously been given [8]. With this in mind, limiting staff exposure during administrations is of increasing importance.

Various methods are employed to administer radiopharmaceuticals. One example dispenses ^{131}I mIBG directly from the vials in which it is delivered by a burette to allow dilution. This eliminates the need for radiopharmacy to prepare a syringe, reducing dose to radiopharmacy staff. However, this system is large, making it inconvenient to store and transport. It is complex, requiring additional training for staff, is designed for use with only one radioisotope and requires proprietary dispensing kits for every use that add significant cost and make the system unusable in the case of a supply shortage.

Treatments can also be delivered using a syringe pump enclosed within a lead brick castle. This cost effective solution uses standard equipment. However, to see the pump controls and infusion progress, shielding must be removed, exposing the operators. Because of the proximity of the activity to the pump controls, even greater operator (particularly finger) dose is incurred when setting up and adjusting the infusion. Pump design (e.g. if it is front loading) may make it difficult to encase, whereas the size and weight of the shielding needed may present hazards, particularly with transportation.

The InfuShield system is relatively compact and easy to transport. The use of standard equipment means staff are familiar with the components and costs are minimized. The segregation of shielding and pump allows for the use of any pump, whatever its design and dimensions. It also grants the user full access to the pump and its controls so that the infusion can be monitored and adjusted, while simultaneously providing a high level of shielding.

Flow rate

The tests carried out show that InfuShield has little effect on the flow rate. The small differences noted show no distinct pattern, being evenly split between increasing and decreasing the flow. Even the largest difference (1.29%) in flow rate compares favourably to the system

accuracy of $\pm 2\%$ typically by volume, specified in the pump manual [9].

Testing did show an increase in the variance of the flow rate over the course of the infusions. However, even the largest measured variance (2.99%) is only slightly larger than the system accuracy and was considered insignificant by our clinical staff.

Occlusion alarm

The testing showed that occlusion alarms are delayed by the use of InfuShield. It is believed that this is due to the increased volume in the system and the compressible bungs inside the two additional syringes. The clinical team considered the time to alarm of no clinical significance, so long as the maximum pressure could not exceed the limit set on the pump. The occlusion test demonstrated that despite a longer build-up, the alarm still functioned correctly once the maximum pressure had been reached.

Shielding

The results of the ^{131}I dose rate measurements are in good agreement with the theoretical attenuation levels calculated. The largest difference was for the dose rate measured through the side walls, where the dose measured was double the predicted dose. This is likely to be due to photons scattered from the top and bottom of the container.

A direct comparison of the effectiveness of InfuShield's shielding with that of other administration systems was not possible because of a lack of published data; nevertheless, results do show that doses incurred when transporting, setting up, viewing and adjusting an ^{131}I infusion are 1000 times lower using InfuShield than they would be if the therapeutic activities were driven directly by an unshielded pump. InfuShield also increases the distance from the activity to the pump's controls by ~ 10 -fold. Therefore, finger doses from accessing those controls are 100 000 times smaller. The measurements made with ^{90}Y and the calculated attenuation of ^{177}Lu (Table 1) show that with therapeutic quantities of these isotopes, dose rates will be reduced to negligible levels.

InfuShield was designed to reduce staff doses as much as practicable while taking into account health and safety considerations. However, the thickness of the shielding was determined by the high energy γ emissions of ^{131}I . Much less lead would be required if only ^{90}Y or ^{177}Lu was to be used. This would considerably reduce the weight of the device and the associated health and safety risks. In the case of ^{177}Lu , 0.7 mm of lead would reduce the dose by a factor of 1000, resulting in a dose of $0.03 \mu\text{Sv/h}$, 50 cm from a 3700 MBq source (Rad Pro Calculator, version 3.26; Ray McGinnis; <http://www.radprocalculator.com>). This should also provide adequate shielding for ^{90}Y , as the inner layer of Perspex will effectively stop the β emissions (10.3 mm range in Perspex) resulting in a

Bremsstrahlung spectrum, the majority of which will be attenuated by the lead [10].

Staff doses

Good practice when implementing a new radiation procedure is to set a staff dose constraint equal to the public dose constraint of $300 \mu\text{Sv/year}$ [3]. At our institution we carry out an average of six ^{131}I mIBG administrations per year, with staff typically spending less than an hour, per administration, in close proximity to InfuShield. Using the reported dose rates we calculate that annual staff doses from InfuShield, for this procedure, are less than $10 \mu\text{Sv}$. Measured doses, however, show that administering staff receive $353 \pm 144 \mu\text{Sv}$ annually (six procedures). The additional dose measured is principally because of radiation emanating from the patient. The large range in the doses received and their poor correlation with the administered activity result from variations in the level of nursing care required by the (mainly paediatric) patients. Despite this, received doses compare well with other published data [11]. Further optimisation should focus on reducing staff doses received from patients. Doses to radiopharmacy staff [12] might also be reduced through the use of automated dispensing systems.

Clinical use

The InfuShield device was approved for use by our medical devices department and lead infection prevention nurse as well as the relevant nuclear medicine consultants and nursing staff. A standard operating procedure was developed and the device has now been used to deliver over 200 ^{131}I mIBG and ^{90}Y DOTATATE therapies. It has not been used to deliver any ^{177}Lu therapies as our department does not presently carry out this treatment.

Conclusion

The InfuShield system enables therapeutic radionuclide therapies to be administered from a fully shielded syringe using any commercially available syringe driver and intravenous line configuration. The separation of the pump from the radioactive therapeutic agent allows for effective shielding while simultaneously allowing easy access to the pump controls and a clear view of the pump, its display and the progress of the infusion. The dose rates measured with ^{131}I and ^{90}Y show it to be suitable for a wide range of isotopes including ^{177}Lu .

The system helps to achieve as low as reasonably practicable absorbed staff doses, during radionuclide therapy treatments that are functionally equivalent to routine, syringe pump driven, infusions. InfuShield is a simple and safe radioisotope infusion solution.

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Conflicts of interest

There are no conflicts of interest.

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